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JANUARY, 1930

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NOTICE

INTERNATIONAL PEDIATRIC CONGRESS

Announcement regarding the Second International Pediatric Congress, to be held in Stockholm, August 17 to 20, will be found in this issue, p. 185. Previous announcement appeared in the December issue, p. 1280.

1930 SUBSCRIPTIONS NOW DUE

The pink slip which will be found in this issue is a notification that subscriptions for the current year are now due and payable. Those who have already paid for 1930 naturally will disregard the notice.

All of the periodicals published by the American Medical Association are listed on the pink slip, for the convenience of those who subscribe for more than one. The names of the journals desired may be written on the blank lines, or a check mark may be placed in front of the names as listed. The entire amount of the subscriptions for the various publications thus may be covered by one check or draft and sent with the pink slip.

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American Journal of Diseases of Children

VOLUME 39 JANUARY, 1930 NUMBER 1

THE NATURE AND USES OF LYSED TYPHOID VACCINES *

JOSEPH CARONIA, M.D.
SAN FRANCISCO

Up to a few years ago, the therapy for typhoid fever wandered in a maze of vague empiricism. To the person's bodily resistance, almost unhelped, was entrusted the task of aiding his recovery. At best, the only available aid lay in an irrational therapy, or equally irrational dietetics. The first attempts at chemotherapy and serotherapy were such failures that, after short trials, these were abandoned so that medical men were led to renounce all attempts at specific therapy. Then came the advent of vaccinotherapy, an advent which reopened the subject.

I shall discuss the vaccine therapy for typhoid and paratyphoid fever, with special emphasis on lysed vaccines.

From Di Cristina's [1] first experiments in twenty-one cases of typhoid fever, made in 1916, and my own which followed during the same year,[2] in which I studied forty-six cases of typhoid and paratyphoid fever, up to the present time, many experiments in the use of lysed vaccines have been made with uniform success. I could say here, in short, that my experiences with lysed vaccines during the past ten years, as well as those of other observers, prove that these preparations supply the foundation of a method of vaccinotherapy which, up to now, has given the most constant results.[3]

Kharina-Marinucci,[4] Luna,[5] De Finis,[6] Ronchi,[7] Barbara and Sabatini,[8] Mallardi,[9] Arcangeli,[10] Nastasi,[11] Tüdös,[12] Vasile,[13] Lucherini,[14]

* Submitted for publication, Aug. 17, 1929.

*From the George Williams Hooper Foundation for Medical Research, University of California.

1. Di Cristina: Pediatria, 1916, no. 1. 1917, no. 1.
2. Caronia, Joseph: Atti d. r. Accad. med.-chir. di Napoli, 1916; Pediatria, 1917, no. 1.
3. Caronia and Di Cristina: Atti d. Cong. pediat. ital., Trieste, 1920.
4. Kharina-Marinucci, R.: Pediatria **28**:641 and 689, 1920.
5. Luna, F.: Pediatria **28**:706, 1920.
6. De Finis, G.: Pediatria **31**:11, 1923.
7. Ronchi, A.: Pediatria **32**:377, 1924.
8. Barbara and Sabatini: Pediatria (Archivio), 1925.
9. Mallardi: Monograph, Pediatria, 1920.
10. Arcangeli: Lectures published by Rivista Ospedaliera, Rome, 1925.
11. Nastasi: Gior. di med. mil., 1925 and 1927.
12. Tüdös, A.: Jahrb. f. Kinderh. **110**:24, 1925.
13. Vasile: Pediatria, 1926.
14. Lucherini: Riforma med., 1917.

Costanzi,[15] Fr, De Bonis [16] and others have published in various places records of more than 1,000 cases. To the cases reported by these authors may be added several thousand more occurring in the practice of various physicians in different parts of Italy. The vaccine was furnished gratuitously to these practitioners by the pediatric service at Palmero, Naples and Rome.

A study of these numerous observations leads to the conviction that in almost all of the cases the lysed vaccine prevents a fatal outcome, and that its use shortens the duration of the disease from an average course lasting from thirty to forty days, to one that terminates within from fifteen to twenty days; furthermore, under its influence the number and severity of complications are reduced and recurrences are fewer, while no new inconveniences or dangers are encountered when it is employed. Some failures have been reported, but these will be found almost inevitably to have happened in the case of persons coming under treatment at an advanced stage of the disease, with the patient gravely exhausted, or else already the subject of serious complications. It is probable that the timely use of the vaccine and a better technic in its employment would have reduced this small proportion of patients unsuccessfully treated to almost nothing.

One may say that typhoid infections have supplied the testing ground for almost all the experiments underlying vaccinotherapy. From the first uncertain attempts of Fränkel and Petrusky to the brilliant experiments of Ishikawa, who was the first to use the intravenous route, and then on to the present rational use of lysed vaccines, there has been an unbroken series of efforts aiming to solve the problem of producing induced immunity by the use of the vaccines.

EXPERIMENTAL WORK

The technic of preparation of lysed vaccines that I have adopted is one that attempts, as far as possible, to follow the natural processes of cure as they develop in the infected person. The procedure is simple: Using a liquid medium, a culture is made from various strains of Eberth's bacillus. To this culture several additions of small quantities of typhoid convalescent blood are made, in an amount equal to from 2 to 3 per cent of the total volume of the culture. The culture is then held at a temperature of 37 C. until lysis of all, or nearly all, the bacteria is accomplished; when the liquid portion of the culture becomes clear, this is separated from the sediment, phenolized and used as vaccine. In this way, most of the bacilli which have recently matured, together with those which are on their way to maturity, undergo lysis because of the influ-

15. Costanzi, F.: Diagnosi **8**:49, 1928.
16. De Bonis: Rin novamento me Iico, Napoli, 1925.

ence of the added serum. In this way there is created a vaccinal or desensitizing substance of high concentration with a constant titer, and read for use. Moreover, the vaccine is almost free from deleterious elements.

When used by the endovenous route, the dose of this vaccine runs from 0.5 to 1 cc.; when intramuscular or subcutaneous injections are given, the dose runs from 1 to 3 cc. The dose is progressively increased and is given every alternate day, or every third day up to the appearance of defervescence.

Because of the analogy, I may be pardoned for digressing here to say that by using slight modifications of this technic, I have been able to prepare vaccines of similar efficiency to use against various other germs. Such a vaccine I have introduced for the treatment for undulant fever; it has been used in several hundred cases of that disease, and it has proved to be equally as successful as the typhoid vaccine; certainly it is a far better remedy than any other therapy available against that tenacious infection.

The effect of the typhoid and paratyphoid vaccine is more or less prompt; a single injection can bring about a rapid resolution of the disease by crisis in less than twenty-four hours; on the other hand, resolution may be slow and by lysis, lasting through as much as a week and needing several injections to accomplish a cure.

When the vaccine is given intravenously, prompt resolution by crisis is frequent, while when subcutaneous or intramuscular injections are made, resolution is more apt to be by lysis.

When resolution is rapid, there is a notable change in the clinical picture, together with a more or less characteristic reaction. For example, on the ninth or tenth day of illness, a patient with typhoid fever is in a comatose state, with profound pallor, sunken eyes, coated tongue, distended abdomen, rather hurried respiration and a slow or dicrotic pulse, with a rise in temperature that reaches 39 or 40 C. (102.2 or 104 F.). If an intravenous injection of 0.5 cc. of lysed vaccine is made into the patient, within an hour one will see an intense, sometimes even startling, reaction of the anaphylactic type. The pallor of the face is accentuated; the region about the lips may become cyanotic; the pulse grows more rapid and the respiration is accelerated; the extremities become cold, while violent shivering occurs. The temperature falls to 35 or to 37 C. (95 or 98.6 F.); this collapse is of short duration, lasting for not more than ten or fifteen minutes; then the temperature begins to trend upward and to reach a point higher than that before the drop began. In the meantime, the pallor passes and the face flushes a rosy red; the respiration becomes calm and regular, and the pulse becomes full and frequent. The hyperpyrexia lasts from ten to fifteen hours, then it begins to abate; meanwhile the patient's eyes become clear, the

mouth moist, the tongue clean, food and drink are accepted and consciousness is restored. After twenty-four hours the temperature descends to normal limits, and every aspect of the patient alters for the better, with sensations and consciousness aroused, clear eyes, regular respiration, regular pulse, clean mucous membranes and no more anorexia. It sometimes happens that from this time onward no more morbid manifestations arise to disturb the sick person, who passes through a brief convalescence to reach complete restoration (chart 1).

In the majority of cases, however, during the succeeding days there appears a return of the fever, which diminishes progressively and

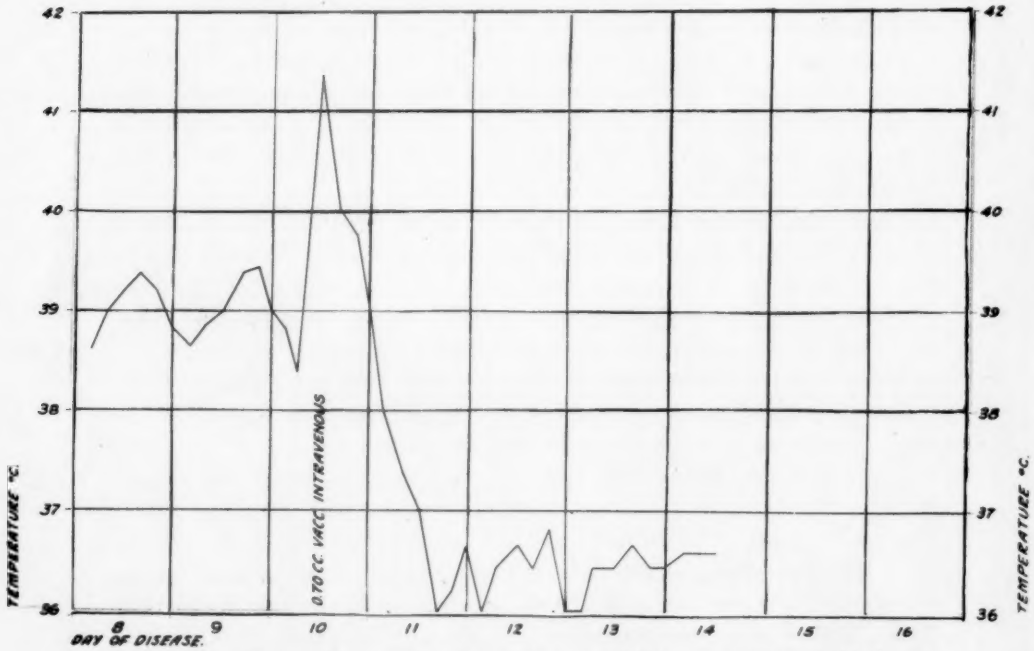

Chart 1.—Temperature curve of a patient, aged 7 years, with typhoid fever. Crisis occurred after an intravenous injection of lysed vaccine.

occurs without reappearance of any of the other symptoms. This fever may disappear within a few days without the need for more treatments (chart 2), or it may become so persistent that further injections of vaccine become necessary (chart 3).

There are still other cases, especially those that resolve very slowly, in which one sees little or no appreciable improvement of the symptoms and only a slight remission of the fever. Under such circumstances, it becomes necessary to give a few more injections of the vaccine at intervals of from two to three days before a complete clearing up of the symptoms is accomplished. In cases of this sort, each injection of

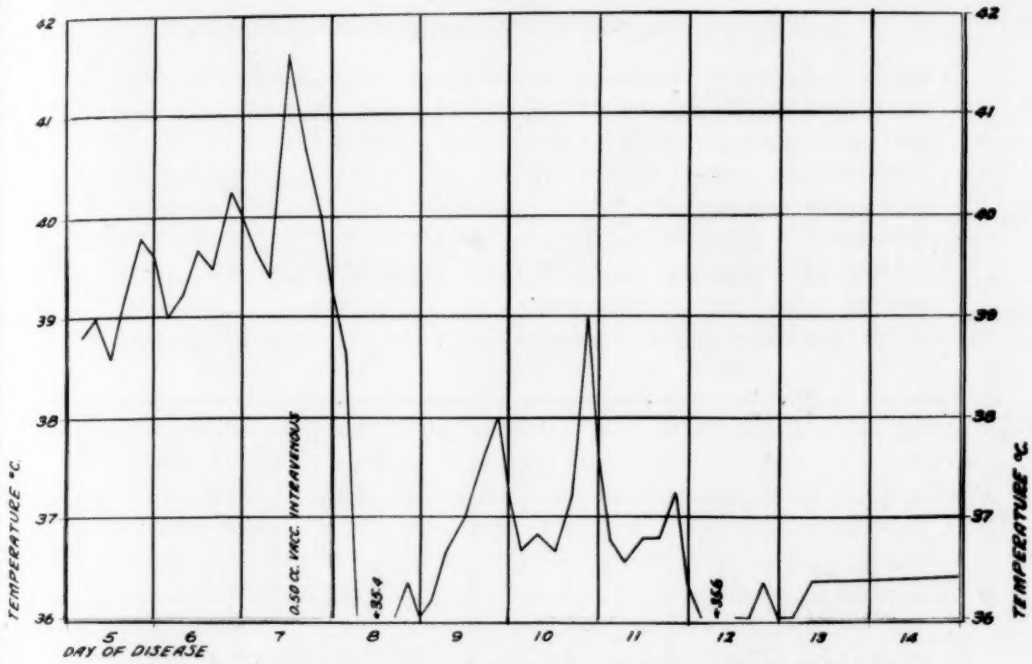

Chart 2.—Temperature curve of a patient, aged 6 years, with typhoid fever. Crisis occurred after an intravenous injection of lysed vaccine.

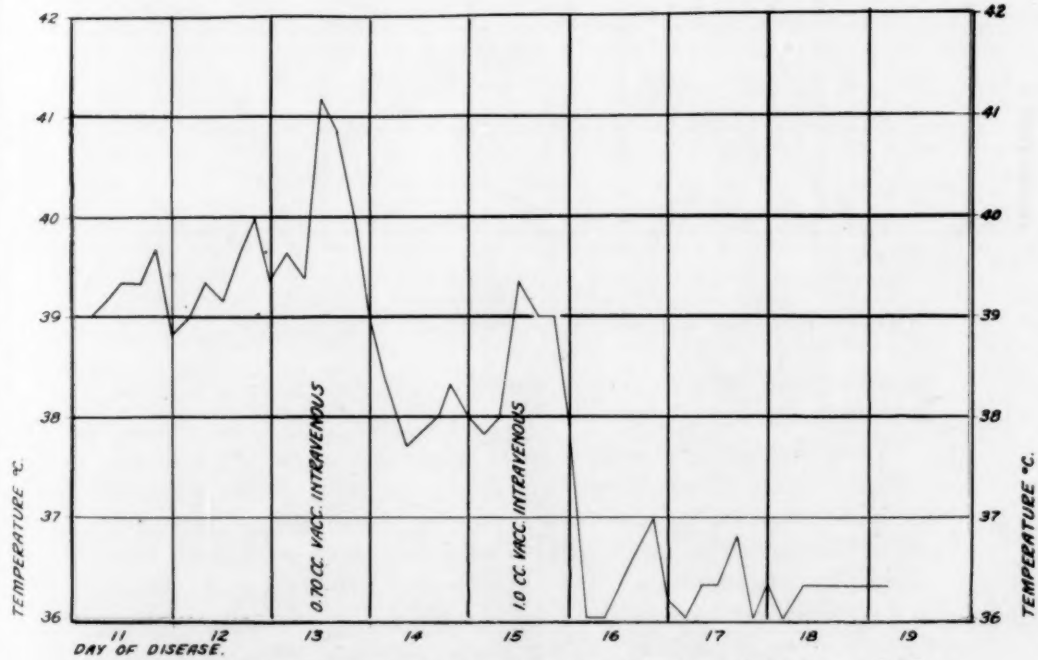

Chart 3.—Temperature curve of a patient, aged 30, with typhoid fever. Crisis occurred after two intravenous injections of lysed vaccine.

vaccine, even when a maximum dose is given, is followed by a reaction less intense than that produced by the preceding dose; at the same time the temperature swings less widely, falling not so low, nor climbing quite so high; its remissions are more certain and more prolonged and at the same time there is a steady improvement in all the other symptoms (chart 4).

As I have said, this behavior is more readily observable in patients who have been treated by intramuscular or subcutaneous injections; certain cases may fail to show any result after the first two or three

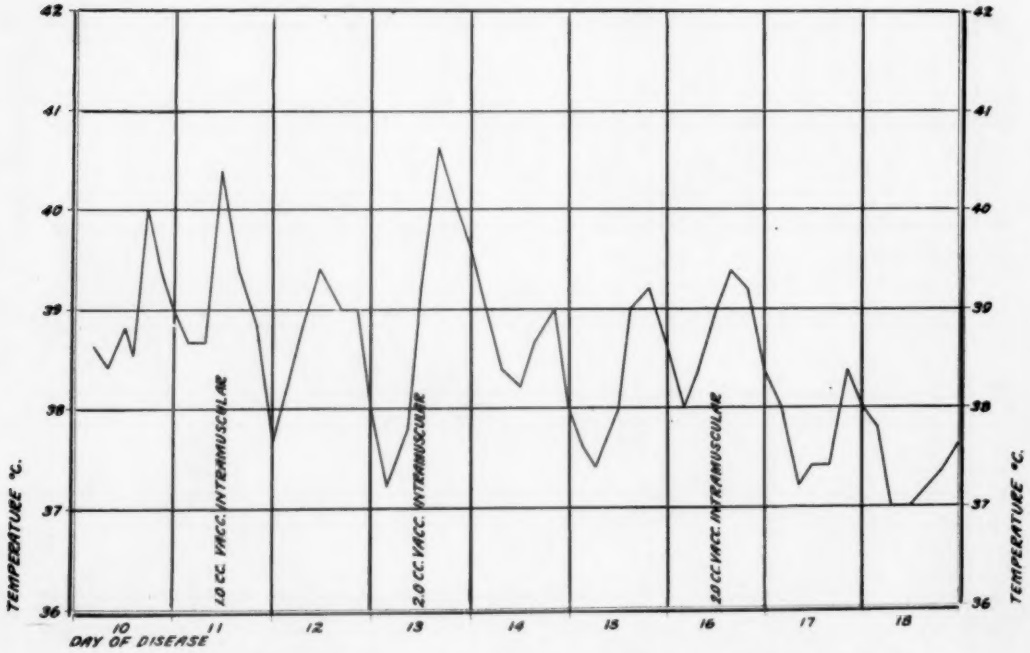

Chart 4.—Temperature curve of a patient, aged 5 years, with typhoid fever. Lysis took place after three intramuscular injections of lysed vaccine.

injections, and yet may resolve with a typical crisis after a third or fourth injection.

These modifications of the clinical phenomena are accompanied by variations in the various internal functions of the body. When studying the blood taken during reaction, one observes that in the earlier stages the number of red and white cells is diminished; this is particularly true of the polymorphonuclears. At a second stage it will be found that there is a slight red cell increase and a leukocytosis with special augmentation of the polymorphonuclears, and also that young forms are being thrown out plentifully into the blood stream. In contrast, the indexes of immunity give no evidence of variations or, at the most, show hardly appre-

ciable oscillations. The amounts of amboceptor and of agglutinin may be slightly lessened, or may remain unaltered. The phagocytic power appears to become augmented, but only slowly. At the height of the reaction, the leukolytic power of the blood serum is definitely increased.

Often, the pathogenic bacteria do not disappear from the organism, not even during convalescence, nor yet when the cure is completed. Under these circumstances the bacilli behave as saprophytes toward the patient.

Of course, the different patients subjected to the treatment, within certain limits, show the greatest variations in the mode of response to treatment. These variations occur in proportion to the period of the disease, the virulence of the infecting germ, the condition of the patient's bodily defenses and his native resistance.

The more promptly the vaccine is employed, the more prompt and certain are the results; at any stage of typhoid fever it is a remedy of definite value, provided, however, that it is given before all the patient's resistance has been exhausted. There are no contraindications to the use of the method. When confronted by a patient who suffers also from cardiac or renal disease, the physician must be cautious in choosing the size of the dose to be given, and he should prefer the subcutaneous or intramuscular rather than the intravenous route for the injection.

For the treatment for paratyphoid infections, either A or B, it will be found that the lysed antityphoid vaccine exerts the same curative influence as it has when used to combat the true Eberth infections.

How do the lysed vaccines exert their curative action? In the present state of knowledge, no precise answer to this question is possible; the most that can be done is to point out certain facts that can be used as the basis of hypotheses more or less near the truth.

One must look to the more recent conceptions which consider the clinical pictures of various illnesses and infections to rest on a basis of hypersensibility of the animal organism to heterologous proteins. In the case of typhoid infection, the hypersensibility of the body tissues is to the protein of the bacillus of Eberth. The action of the lysed vaccine may be thought of as a rapid process of desensitization analogous to the slower process of natural healing. The best proof of its desensitizing nature lies in the fact that each equal dose of the vaccine given successively produces less reaction than the one before, so that by the time cure is accomplished, no reaction shall follow the injection of such a dose. The mechanism of this process of desensitization remains obscure. One may exclude any explanation that brings the matter into relation with the factors of immunity as they are known at present. It is possible that the subject may become clearer when one comes to know more about the various phenomena that influence colloidal equilibrium. For among

these phenomena one may find those influences that neutralize the damaging effects of toxins which arise from disease-producing germs.

Whatever the nature of the action of the lysed vaccine may be, the clinical results are important. These results induced Arcangeli, after his experience with 174 cases in the Policlinic Hospital at Rome, to write: "In regard to the specific treatment of typhoid fever, I am convinced that we should give the preference to vaccines and, among these, to the lysed vaccines. I believe that the time has passed when we should entrust the cure of the patient to symptomatic treatment and to the patient's own natural resistance."

CONCLUSION

In closing my short presentation, I wish to say that I have chosen to avoid new arguments for the use of lysed vaccines in the treatment for typhoid and paratyphoid fevers, because I think that it is more useful once again to emphasize the utility of vaccinotherapy in spite of the discord and skepticism which at present seem to dominate medical thought on this subject. This discord and skepticism result largely from the multiplicity of technically unsound methods that have been adopted during recent years, methods that have succeeded in confusing the principles of vaccinotherapy with those of proteinotherapy.

It is to be hoped that in the vast, well supported fields of North American medical research, there will be established studies on vaccinotherapy, studies subjected to those rigorous modern scientific criteria which dominate in the United States. For only from such studies can many of the perplexing questions about vaccinotherapy be definitely answered.

AN INVESTIGATION OF SOME OF THE FABRICS USED IN THE MANUFACTURE OF UNDERCLOTHING*

CHARLES E. SNELLING, M.B.
AND
ALAN BROWN, M.B.
TORONTO, CANADA

In 1926, Faber and Haddon published some interesting results on investigation of relative value and advantages of the various fabrics used in infants' underclothing. In the present paper are reported the results of a study of the different properties of the various fabrics used in the manufacture of infants' underclothing and diapers. The following points are considered:

1. Power of heat retention.
2. Moisture absorption and loss.
3. Porosity.
4. Skin irritation and allergy.
5. Cleansing strength and durability.
6. Relative cost.

The materials were all obtained direct from the manufacturer, being made up especially for this investigation. They were fabricated uniformly, and the raw material used in the manufacture was definitely known. The fabrics studied were various woolens, wool and cotton combined, cottons and rayon. The diaper materials were canton flannel, flannelet, bird's eye and knitted diapers.

The thread of yarn that is the basis of all these fabrics is obtained from cotton or wool by a number of processes, namely, cleansing, combing, carding, drawing and finally spinning. In the cheaper grades of fabric, one or more of these steps are omitted. Mercerized yarn is produced by the subjection of combed cotton to a strong caustic. Rayon is produced by the dissolving of cotton fibers or wood pulp in a chemical solution. This is blown through fine nozzles and the streams are reprecipitated as strands which are twisted together to form a yarn or thread. Combing produces a much better yarn, removing the short fibers in both cotton and wool and removing the husks in cotton. The best woolen yarn is worsted in which the fibers are drawn many times before the yarn is spun, so that the fibers all run parallel.

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* From the Laboratories and Wards of the Sub-Department of Paediatrics, University of Toronto and of the Hospital for Sick Children.

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Knitting is a series of interlocking loops and has variations which are made by variations in the way the loops are interlocked. The usual ones are ribbed knit and flat knit. Ribbed knit is more elastic and is made to be worn stretched from 15 to 20 per cent. Flat knit is made to fit at the same size.

Fleece-lined underwear is made of a two-faced fabric, the outer layer being closely knitted, and the inner face loosely knitted. The inner face is then subjected to a strenuous brushing which fuzzes up the surface and produces the soft inner lining of fleece-lined underwear. It is always made of cotton.

A new type of fabric produced as a result of these experiments is somewhat the same as the fleece lined. It is produced by making an outerface of wool and an inner of cotton and is called a two layer fabric. The advantages of this fabric will be shown in the experimental work.

The woven fabrics usually used in diaper materials are made by two sets of threads that run at right angles to each other alternately passing above and below the threads running in the other direction. Variations in the appearance of this are produced by the groupings of the threads. Flannelet and canton flannel have the fuzzy surface produced by brushing—the same as in fleece-lined underwear.

Bleaching is brought about by the fabrics being treated with various chemical solutions that change the color, remove the resins, oils and gums, and if carried too far, weaken the garment. Shrinking is done on all garments by treatment with steam or boiling.

RETENTION OF HEAT

The ability of a fabric to retain heat was investigated in two ways:

1. The first method was to cover liter bottles with the fabric under investigation. The bottles were filled with hot water, and the cork and thermometer replaced; the temperature was taken and again recorded in one hour. The fabric covering the bottle in which there is the least fall in temperature must obviously be the best retainer. As a control, the temperature was recorded in an uncovered bottle.

The bottles were rinsed three times with hot water to heat the glass and overcome the initial sharp fall due to the cold glass. The thermometers were at the same level; the water was not agitated, and the bottles were placed 2 feet apart to overcome radiation from one to another. Different room temperatures caused different results, but the relative fall was always in the same proportion. The initial temperature was 70 C. This experiment was carried out in three groups, and the results are shown in tables 1, 2 and 3. These results definitely show that wool does not allow the heat to escape as readily as the other fabrics. Mixtures of wool and cotton increase the fall in proportion to the amount of cotton. Unbleached cotton retains the heat the best

of the cottons, and rayon is poor in comparison to all the others. Canton flannel in the diaper materials is warmer than the others.

2. The second method for determination of heat retention was the observation of the effect on the human subject. A sensitive electrical skin thermometer was used in which readings of 0.01 C. could be made.

TABLE 1.—*Heat Retention: Fall in Temperature of Bottles Covered by Ribbed Knit Fabrics, Fleece-Lined and Rayon Fabrics for One Hour*

Fabric	Average Fall (Centigrade)	Per Cent Fall	Calories Lost	Calories Retained
Ribbed knit:				
1. Wool	11.9	100	11,900	58,100
2. Wool and cotton (equal parts)	13.0	108.3	13,000	57,000
3. Unbleached cotton	13.7	114.9	13,700	56,300
4. Mercerized cotton	14.8	123.4	14,800	55,200
Fleece-lined	13.1	110.4	13,100	56,900
Rayon	15.8	132.0	15,800	54,200
Control	17.9	149.0	17,900	52,000

TABLE 2.—*Heat Retention: Fall in Temperature of Bottles Covered by Flat Stitch Knit Fabrics and Diaper Materials for One Hour*

Fabric	Average Fall (Centigrade)	Per Cent Fall	Calories Lost	Calories Retained
Flat stitch knitted				
1. Wool	10.2	100	10,200	59,800
2. Bleached cotton	13.6	129	13,600	56,400
Fleece	12.8	120.6	12,800	57,200
Canton flannel	10.7	106	10,700	59,300
Flannelet	12.3	120	12,300	57,700
Bird's eye	12.8	125	12,800	57,200

TABLE 3.—*Heat Retention: Fall in Temperature in Bottles Covered for One Hour by Ribbed Knit Fabrics, Wool, Wool and Cotton Combined by the Usual Method, and Wool and Cotton Combined by Two Layer Method*

Fabric	Average Fall (Centigrade)	Per Cent Fall	Calories Lost	Calories Retained
Wool	11.0	100	11,000	59,000
Wool and cotton (usual)	11.9	108.1	11,900	58,100
Two layer *				
Number 5	11.4	103.6	11,400	58,600
Number 2	12.3	111.1	12,300	57,700
Number 1	12.2	111.0	12,200	57,800

* Two layer fabrics all approximately 50 per cent cotton and wool. Number 1 was 5 per cent lighter than wool, or wool and cotton. Number 2, same weight as wool, or wool and cotton. Number 5, 15 per cent heavier than wool, or wool and cotton.

The anticubital fossae had the same temperature, were the warmest areas on the arm and could easily have the thermometer put in position by keeping the elbow flexed to a right angle. A sleeve of the fabric tested was placed on one arm and one of another fabric on the other. After five minutes, readings were taken of each arm. The fabric was then changed to the opposite arm, and duplicate readings were obtained. Because the thermometer was so sensitive, it was found necessary to make the determination by simultaneous comparison, as indicated previ-

ously, rather than by the use of a complete garment and then changing. The results of this work are shown in table 4. They indicate that wool retains heat better than cotton and that rayon is the least warm. When this experiment was carried out, the child was asked to indicate which fabric was the warmer of the two being compared, and in all cases indicated the same one as the thermometer except in the case of the fleece-lined, which was given the preference over the others.

TABLE 4.—*Average Temperature of Skin of Thirty Consecutive Determinations Under Each Fabric Used on the Arm as a Sleeve*

Fabric	Average Temperature of Arm (Centigrade)
Wool (flat stitch)	35.25
Wool (ribbed)	35.15
Wool and cotton	34.97
Unbleached cotton	34.75
Fleece-lined cotton	34.50
Bleached cotton	34.50
Mercerized cotton	34.43
Rayon	34.08

TABLE 5.—*The Number of Cubic Centimeters Absorbed Per Gram of Fabric After Five Minutes' Submersion in Water: Average of Five Determinations*

Fabric	Cubic Centimeters Absorbed
(*a*) Diaper materials	
Flannelet	3.73
Bleached cotton (knitted)	2.89
Bird's eye	2.3
Canton flannel	1.25
(*b*) Underwear fabrics	
Rayon	1.85
Fleece	1.32
Bleached cotton	2.89
Mercerized bleached cotton	2.18
Unbleached cotton	0.59
Wool and cotton	0.95
Wool	0.85
Two layer fabrics—number 5	2.0
number 2	1.7
number 1	1.3

ABSORPTION AND EVAPORATION OF MOISTURE

Determination of Total Absorption Per Gram of Fabric.—Pieces of fabrics of the same square area were weighed and then immersed in a beaker with a known quantity of water for five minutes. They were suspended over the beaker, and the excess was allowed to drip. The water in the beaker was measured, and the amount absorbed by the cloth determined. This divided by the weight of the fabric gave the number of cubic centimeters absorbed per gram of fabric. The results are shown in table 5.

The results show some interesting facts. Of the diaper fabrics, flannelet absorbs the most, knitted bleached cotton next and canton flannel absorbs poorly. Among the underwear fabrics, bleached cotton

absorbs the best, rayon fairly well, wool poorly and unbleached cotton has the least. In the two layer fabrics, the amount of absorption is in proportion to the amount of cotton present.

Rapidity of Absorption.—A drop of water was placed on each side of the fabric, and the time taken for it to disappear recorded. The results are shown in table 6.

In the diaper fabrics, knitted bleached cotton and bird's eye showed immediate absorption; flannelet took some time for absorption, and canton flannel did not show any disappearance of the drop. Rayon and bleached cotton showed immediate absorption, mercerized cotton fairly rapid absorption and the other fabrics did not show any absorption

TABLE 6.—*Rapidity of Absorption of a Drop of Water Placed on the Surface of the Fabric*

	Fabric	Time Taken for Drop to Disappear
(*a*)	**Diaper fabrics**	
	Bleached cotton (knitted)	Immediate
	Bird's eye	Immediate
	Flannelet	Eighteen minutes
	Canton flannel	Drop remained till evaporation
(*b*)	**Underwear fabrics**	
	Rayon	Immediate
	Fleece-lined	Drop remained till evaporation
	Bleached cotton	Immediate
	Mercerized bleached cotton	Fourteen minutes
	Unbleached cotton	Drop remained till evaporation
	Wool and cotton	Drop remained till evaporation
	Wool	Drop remained till evaporation
	Two layer fabrics	
	Number 1, wool side	Drop remained till evaporation
	cotton side	Drop remained till evaporation
	Number 2, wool side	Drop remained till evaporation
	cotton side	Drop remained till evaporation
	Number 5, wool side	Drop remained till evaporation
	cotton side	Thirty seconds

except on the cotton side of one of the two layer types in which bleached cotton was used.

Capillary Action of Fabrics.—Fabrics were cut in strips about 2 cm. wide in each direction of the knit or weave, and suspended in a basin of water as a wick. These were left for thirty minutes, and the distance the water had ascended was measured. The results are shown in table 7.

The distances were the same in the two directions of the fabric. Bleached cotton had the greatest capillary action, and the moisture traveled to the top of the strips used; bird's eye was next, flannelet had little and canton flannel did not have any capillary action. The underwear fabrics, except bleached cotton, one two-layer fabric with bleached cotton on one side and rayon, did not have any capillary action.

Heat Drop Caused by Evaporation.—Only representative fabrics were used. A piece of fabric was saturated with water, wrapped around the bulb of a mercury thermometer and left for ninety minutes. The results are shown in table 8.

These figures show that the evaporation from wool causes less drop in temperature than a like evaporation from cotton, and that the drop in temperature is somewhat in proportion to the amount of water absorbed.

Evaporation from Fabrics at Saturation.—The total absorption was determined as in 1. The fabrics were hung on a line for one hour and weighed. The dry weight was known, so it was easy to determine the amount of evaporation. Owing to a difference in humidity, variations in the results were obtained but always with the same respective

TABLE 7.—*Capillary Action of Fabrics*

Strips of fabric 2 cm. wide and 18.5 cm. long suspended as a wick in a basin of water for 30 minutes.

Fabric	Height Water Ascended
(*a*) Diaper materials	
Bleached cotton (knitted)	18.5 (top)
Bird's eye	13.0
Flannelet	2.0
Canton flannel	0.0 did not rise
(*b*) Underwear fabrics	
Rayon	12.5
Fleece-lined	0.0 did not rise
Bleached cotton	18.5
Mercerized bleached cotton	0.0 did not rise
Unbleached cotton	0.0 did not rise
Wool and cotton	0.0 did not rise
Wool	0.0 did not rise
Two layer fabrics	
Number 1	0.0 did not rise
Number 2	0.0 did not rise
Number 5	2.5

TABLE 8.—*Fall in Temperature Due to Evaporation*

Fabrics, wrapped on bulb of thermometer saturated with water and left 90 minutes.

Fabric	Drop in Temperature (Centigrade)
Wool	7.0
Bleached cotton	8.5
Rayon	8.5
Flannelet	7.5
Bird's eye	7.5
Canton flannel	6.9

sequence. The figures obtained from averaging three similar days are shown in table 9.

The table shows that the moisture is lost in greater quantities from those fabrics absorbing most, but that a greater percentage of the moisture is evaporated from those which take up water poorly.

POROSITY

A definite experiment to determine the factor of porosity could not be found, as the amounts to be measured are so small that slight variations could not be noted. A wind tunnel was tried with a monometer on the end, and a flame was used to determine whether there was any

further blowing of the flame when one or another of the fabrics were on the wind tunnel. The only conclusions we could draw were that knitted fabrics were more porous than woven, and that the porosity decreased in proportion to the closeness of the weave or knit.

SKIN EFFECTS

Wool is an animal fiber obtained from sheep. It is nature's protection against the elements, and because of this it is adaptable for protection of the human body especially in the form of winter underwear. It is an appendage of the skin, for it is formed of a keratin-like substance. Under the microscope the fiber appears round, kinky and covered with scales. Wool fibers are elastic and will stretch to a great degree without breaking and then return to their original length. The wool fiber also tends to be stiff and springy in the transverse direction

TABLE 9.—*Evaporation Compared with Absorption: Average of Three Similar Days*

Fabric	Evaporation in Cc. per Gm. of Fabric	Total Absorption*	Percentage of Total Absorption
Flannelet	0.9	3.7	24.3
Bleached cotton	0.65	2.9	22.4
Mercerized cotton	0.64	2.2	29.0
Bird's eye	0.6	2.3	26.0
Rayon	0.52	1.85	28.1
Canton flannel	0.5	1.25	40.0
Fleece-lined	0.48	1.4	34.3
Wool and cotton	0.32	0.95	33.4
Wool	0.28	0.8	35.0
Unbleached cotton	0.22	0.59	37.3

* Compare table 5.

as well as longitudinal elasticity. The appearance of the yarn depends on whether woolen yarn or worsted is used. In all the woolen fabrics used in our experiments worsted yarn was used. In the woolen system the long and short fibers are used; they are so handled that the fibers cross and interlace in every direction. This obviously would produce a much greater number of stiff projections to irritate the skin. In the worsted spinning the short fibers are combed out, and the fibers are drawn out and redrawn, doubling and redoubling until the fibers all run parallel; then the yarn is spun. This takes away a number of the projections and makes the fabric more comfortable.

Cotton fibers are vegetable, being obtained from the seed pod of the cotton plant. They are cellulose, of a fine soft texture, and appear under the microscope as curled with thicker edges and flat in the center. The cotton yarn is produced by the parallel drawing out of the fiber, and then spinning. This produces as strong but not as harsh or irritating a fabric as wool; the cotton fibers are not so springy and stiff. They also are softer and have not the small scales. These are the two factors that make wool so irritating to the skin.

Rayon fibers are long strands of the product of cellulose with various chemicals. They are smooth; they have a luster, and look perfectly round. When made into yarn they appear like a shiny smooth twisted cord with few of the fibers extending out. This makes a smooth fabric without irritating qualities.

To overcome the irritation of wool, a garment with cotton on the one face and wool on the other will work well. This is called the two layer fabric. It has also been found in the hospital that patients with eczema do not do well with wool, and some are definitely allergic to this fabric. The two-layer fabric improves the condition of the skin in this type of patient.

CLEANSING, STRENGTH AND DURABILITY

Cleansing.—A good method was not found to test the cleansing of the various fabrics, except in the experience of the laundry. Wool is not as easy to launder. The fabrics from reliable manufacturing houses are preshrunk and will stand the usual laundering process without shrinking. However, they will not stand boiling or being rubbed with strong alkali soaps, because this as well as shrinking, materially lessens the strength of the garment. Cotton has the advantage that it may be boiled and sterilized, but when strong alkali soaps and bleaching powders are used in the laundering, its strength also is materially lessened. Rayon must be handled with care like wool when it is washed; it has a tendency to stretch when wet, and is much weakened by being moist.

The fabrics were all put through the laundry here and were subjected to a thorough process. The ribbed knit cottons had stretched from one-third to one-half longer. Fleece, canton flannel and flannelet had a large amount of the fuzz worn away and would be all worn off after a few further washings. The woolen fabrics were practically unchanged. The rayon and bird's eye also were unchanged.

Strength and Durability.—Cotton and wool have about the same strength when new. Wool is more durable if laundered properly as cotton in time becomes brittle. This materially decreases the strength. The main disadvantage of wool is the shrinking. This is overcome by the two layer fabric, as the cotton on the inner surface provides a framework to hold it in shape. Rayon is strong, wiry material and stands up well if, as was said before, it is not strained when it is wet. Rayon has one disadvantage in that if a thread is torn as a result of the slipperyness of the yarn it produces a run. The other fabrics do not. As for the diaper fabrics, the durability factor is more important. Flannelet and canton flannel both by washing and scrubbing lose the nap, decreasing their efficiency and also their water absorptive power. This does not occur with knitted fabrics, so that they stand up much better in the long run. The personal experience of families that use knitted diapers show that the knitted variety outwear three sets of the woven.

RELATIVE COST

Information regarding the relative cost and popular demand of the made up garments was obtained from the children's wear department of one of the large department stores.

Plain cotton is the cheapest; cotton and rayon mixed costs slightly more. Wool and cotton, or wool and rayon, is more expensive. Pure wool is next in cost, and silk and wool is most expensive. Rayon and wool is a fine appearing fabric; it is not as irritating, and is in greater demand than other fabrics.

Flannelet nightgowns are the most popular. Wool knitted nightgowns are double the price. Light wool gertrudes are used to a great extent, being worn under the nightgown or dress. The day dress usually sold is made of plain woven cotton.

Bird's eye and flannelet are the most popular and cost about half as much as a knitted diaper. This, however, is probably due to the fact that so far there has not been a great demand for the knitted fabrics for diapers.

COMMENT

The ideal underwear is one combining warmth, ready and rapid absorption, lack of skin irritation and durability with moderate cost. The two layer fabric has all these properties to the greatest extent because of the wool on the outer surface, the heat retention power and durability are greatest; with bleached cotton next the skin, absorption of body moisture and lack of irritation are insured. This two layer fabric is more expensive than cotton, but not as expensive as wool.

The properties to be considered in choosing the most useful type of diaper are ready and rapid absorption, softness, elasticity, durability and relative cost. The knitted bleached cotton diaper absorbs rapidly; it is soft, elastic, and it fits the body. The experience of those using the knitted diapers has shown that they will last for at least three children, and that in that time their efficiency does not decrease. The initial cost is nearly double, but the woven diapers do not usually wear for more than one child. When wet, a woven material is harsh next the skin. The efficiency of the woven diapers with the fuzzy surface becomes much less after a few washings. The woven fabrics will not conform to the shape of the body, but makes the child conform to the shape of the diaper. Thus it can readily be seen that economically, and for relative usefulness, the knitted bleached cotton diaper is a real advance over the woven fabrics.

THE RELATIVE DIGESTIBILITY OF UNSWEETENED EVAPORATED MILK, BOILED MILK AND RAW MILK BY TRYPSIN IN VITRO*

ZONJA WALLEN-LAWRENCE, B.S.
AND
F. C. KOCH, PH.D.
CHICAGO

An extensive literature, covering the effect of heat treatment on the organic and inorganic constituents of milk, on enzymes, vitamins, etc., has accumulated during the past forty years.[1] An equally large clinical literature records the observations of workers in this country and abroad with regard to the relative merits of raw and heated milk as artificial food for infants. Mojonnier,[2] in 1905, reported results of digestion in vitro of raw and heat treated milk by artificial gastric juice which showed that evaporated milk was somewhat more digestible than raw, pasteurized or boiled milk. Hess, Koch and Sennewald[3] have studied peptic digestion of cow's milk and the effect on it of various modifications used in infant feeding, including boiling. They also showed that heat treated milk is more digestible by pepsin in vitro than raw milk, and they concluded that the greatest value of all the milk modifications studied by them may lie in the softer broken curd which exposes a large surface to the digestive juices and in the denaturization of the proteins. Clinical experience confirms these results. Abt[4] stated that clinical observers who have fed raw and boiled milk for an equal number of years are agreed that boiled milk is more readily digested than raw. Marriott and Schoenthal,[5] after an extensive comparative study of unsweetened evaporated milk and ordinary bottled

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* From the Laboratories of Physiological Chemistry, the University of Chicago.

* This work was done during the tenure of a fellowship from the Evaporated Milk Association.

1. Lane-Claypon: Milk in Its Hygienic Relations, New York, Longmans Green & Company, 1921.

2. Mojonnier, T.: The Digestibility of Evaporated Cream, Med. New. **87:** 877, 1905.

3. Hess, J. H.; Koch, E. M., and Sennewald, Z. C.: Peptic Digestion of Cow's Milk, J. A. M. A. **87:**1360 (Oct. 23) 1926.

4. Abt's Pediatrics, Philadelphia, W. B. Saunders Company, 1921, vol. 2, p. 675.

5. Marriott, William McKim, and Schoenthal, L.: An Experimental Study of the Use of Unsweetened Evaporated Milk for the Preparation of Infant Feeding Formulas, Arch. Pediat. **46:**135, 1929.

milk in the feeding of new-born, well, sick and premature infants, recommended unsweetened evaporated milk and enumerated its advantages over ordinary cow's milk for artificial infant feeding. Brennemann [6] from his experiments in feeding sick ward babies, without selection of cases, on simple mixtures of evaporated milk and water, stated, " . . . the immediate result of feeding . . . was the most startling I have ever encountered in more than twenty-five years of hospital experience in feeding ward babies." Other physicians have published similar reports. So from laboratory and clinical evidence, it is agreed that heat treated milk is more readily digested than raw.

THE INCREASE IN TRYPSIN DIGESTIBILITY IS NOT CORRELATED WITH A CHANGE IN THE BUFFER SYSTEM OF MILK

What accounts for this increased digestibility? Since cow's milk is more greatly buffered than human milk,[7] and since evaporated milk or boiled milk is handled by the infant more nearly like human milk, the question may be asked whether a radical change in the buffer system occurs on treatment with heat. It is our experience that it takes slightly more acid to bring a given volume of evaporated milk (diluted 1:2) to p_H 1.9 than it does to bring an equal volume of raw milk to that p_H, suggesting that evaporated milk is not less buffered than raw milk. There is also evidence that heat treatment does not appreciably alter the concentration of soluble inorganic constituents in milk,[8] and this is confirmed by observations on electrical conductivity. Rice [9] has shown that the electrical conductivity of evaporated milk is within the limits ordinarily observed for raw milk. There is also clinical experimentation in progress which may confirm these laboratory observations.[6] So the conclusion must be drawn that a change in the buffer system adequate to account for the altered digestibility of heat treated milk does not occur.

Brennemann [10] in his classic experiments on coagulation of cow's milk in the human stomach has conclusively shown that boiled and evaporated milks form softer, finer curds in the stomach (as well as in vitro) than does raw milk. He has further shown that milk precoagulated with acid, with rennin, or with both, milk treated with lime

6. Brennemann, J.: The Curd and the Buffer in Infant Feeding, J. A. M. A. **92**:364 (Feb. 2) 1929.

7. Marriott, W. M., and Davidson, L. T.: The Acidity of the Gastric Content of Infants, Am. J. Dis. Child. **26**:542 (Dec.) 1923.

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water or magnesia, milk to which barley water is added, and peptonized milk, all have two things in common: they all form a fine curd in the human stomach, and they are universally recognized as more easily digested by both well and ill infants. This raises the question, is the difference in digestibility of raw and heat treated milks a function solely of the nature of the curd?

THE QUESTION OF THE CURD

To throw some light on this question the digestibility, in vitro, of evaporated, boiled and pasteurized milks has been compared with that of whole raw milk. Tryptic digestion has been studied, and since this is carried on in an alkaline medium, the complicating factor of difference in size and consistency of the curd does not enter into the work. The criteria of digestibility have been the increase in total soluble nitrogen and the increase in refractometric readings of the protein-free filtrates before and after a period of digestion.

For our earlier studies unsweetened evaporated milk was diluted with distilled water in such quantity that by macro-Kjeldahl analysis the total nitrogen concentration of the diluted milk equalled that of the raw with which it was to be compared. This was so consistently accomplished by a 1:2 dilution of the evaporated milk that ultimately the macro-Kjeldahl control of concentration was dispensed with as unnecessary. When boiled milk was under consideration, a homogeneous sample of whole certified milk was divided into two portions and one portion boiled under a reflux condenser. Whole pasteurized milk was compared with whole certified milk directly, or a given sample of certified milk was divided and part of it pasteurized. Each sample of milk was adjusted electrometrically to p_H 8.2 using dilute sodium carbonate. As soon as the samples had attained a temperature of 38 C., trypsin was added in graduated amounts to each series of flasks, except to the controls. The total nitrogen concentration was kept equal in all flasks by appropriate additions of water, p_H 8.2. Immediately after the addition of the trypsin a sample was removed from each flask and the proteins precipitated from each sample with trichloracetic acid. The filtrates were analyzed as will be described. The flasks containing milk and trypsin were placed in a vertically rotating shaker in an incubator at 38 C. After four hours of continuous shaking at 38 C., samples were again removed from each flask and the proteins precipitated, as before, with trichloracetic acid. The water clear filtrates were examined at once in the same way as the "zero hour" filtrates.

In all instances, the filtrates were examined with a Zeiss dipping refractometer at 25 C. The increase in the refractometric reading in the "four hour" filtrate over the reading in the corresponding "zero hour" filtrate was taken as a measure of digestion. That this is war-

ranted has been demonstrated by McMeekin [11] for peptic digestion of egg white, and by Helmer [12] for tryptic digestion of casein. However, in the early part of this work the trichloracetic acid filtrates were also analyzed for total nitrogen by the macro-Kjeldahl method. The data from one such experiment are given in table 1. Chart 1 shows these data plotted, with increases in total nitrogen or increases in refractometer readings as abscissae against increasing trypsin concentration as ordinates. Comparison of the two sets of curves confirms the work of McMeekin and of Helmer, showing that the Kjeldahl method could be dispensed with and that the much more rapid refractometric method could be relied on in subsequent work.

TABLE 1.—*Comparison of the Macro-Kjeldahl and the Refractometric Methods for Measuring Tryptic Digestion*

No.*	Cc. Trypsin	Cc. Water	0 Hr. Refr.	4 Hr. Refr.	Increase	0 Hr. Mg. per cent Nitrogen	4 Hr. Mg. per cent Nitrogen	Increase Mg. per cent Nitrogen
1.....	0	5	51.74	51.75	0.01	26.9	25.4	—1.49
2.....	0	5	51.50	51.50	0.00			
3.....	2	3	51.70	55.40	3.70		124.9	98.0
4.....	2	3	51.68	55.35	3.67		122.8	95.9
5.....	3	2	51.62	56.60	4.98		153.4	126.5
6.....	3	2	51.35	56.71	5.36		157.3	130.4
7.....	4	1	51.39	57.72	6.43		176.8	149.9
8.....	4	1	51.52	57.72	6.20		175.7	148.8
9.....	5	0	51.40	58.62	7.22		192.9	166.0
10.....	5	0	51.24	56.68	7.44		204.4	172.5
11.....	0	5	50.25	50.30	0.05		26.2	0.5
12.....	0	5	50.15	50.22	0.07			
13.....	2	3	50.39	51.40	1.01		61.0	35.4
14.....	2	3	50.69	51.51	0.92		61.4	35.8
15.....	3	2	50.55	53.01	2.46	25.7	99.5	73.9
16.....	3	2	50.54	53.01	2.47		100.7	75.1
17.....	4	1	50.15	54.32	4.17		128.4	102.8
18.....	4	1	50.11	54.02	3.91		125.6	100.0
19.....	5	0	50.18	55.27	5.09		147.0	121.4
20.....	5	0	50.31	55.40	5.09		144.7	119.1

* 1 to 10 inclusive gives data for unsweetened evaporated milk diluted 1:1; 11 to 20 inclusive, for raw certified milk.

Following the method outlined, ten samples of unsweetened evaporated milk, representing five different brands bought in the open market, were compared with whole raw milk. Boiled and pasteurized milks were also compared with raw. The results are illustrated in charts 1 to 4, inclusive. A total of 232 separate comparisons of tryptic digestibility of raw and heat treated milk has been run, and in every case the heat treated milk has been digested more readily than the raw. The degree of change in digestibility appears to be a function of both the temperature to which the milk is heated and the length of time during which it is held at that temperature.

11. McMeekin, T. L.: Studies on the Purification of Pepsin, Thesis (Ph.D.), University of Chicago, 1925.

12. Helmer, O. M.: A Study of Trypsin and Its Activation by Enterokinase, Thesis (Ph.D.), University of Chicago, 1927.

That the physical character of the curd is an important factor in the digestibility of milk by pepsin in vitro and in the human stomach cannot be doubted. But these tryptic digestions of raw and heat treated milks also show a marked difference in digestibility even though here the size and consistency of the casein curd have not been a complicating variable. Possibly other differences exist beside the physical character of the curd, which in part may explain the better ease with which milk when boiled or evaporated is handled in digestion.

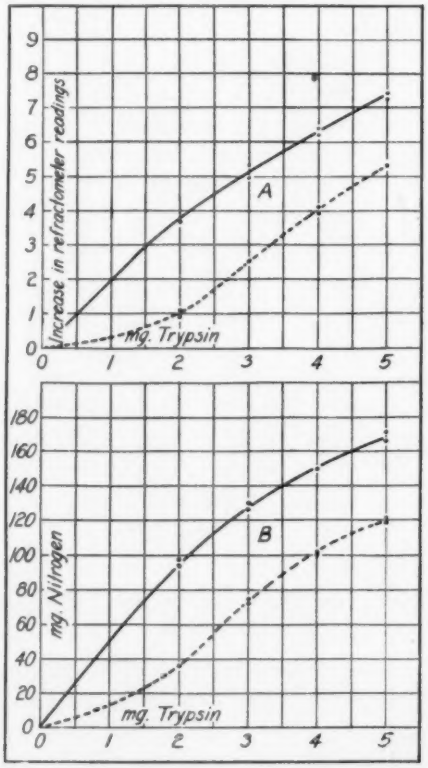

Chart 1.—The solid line indicates curve for evaporated milk; the broken line that for certified raw milk. *A* indicates increases in digestion when using increasing trypsin concentrations and measuring the results refractometrically. *B* indicates the same increase in digestion measured by the increase in total soluble nitrogen expressed in milligrams per hundred cubic centimeters of filtrate. The time of digestion was four hours. For further data see table.

THE DIGESTIBILITY OF THE CASEIN MOLECULE IS NOT ALTERED BY HEAT

It has been suggested that under the influence of heat the casein molecule is changed so as to alter the effect of the digestive enzymes

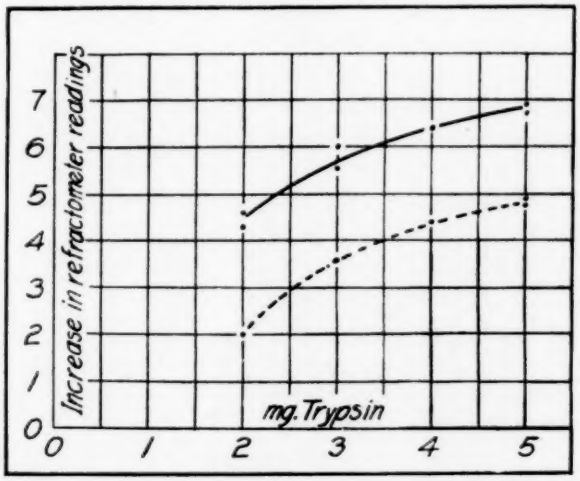

Chart 2.—The solid line indicates curve for certified milk which has been boiled for five minutes; the broken line, that for certified milk not boiled. The time for digestion was four hours.

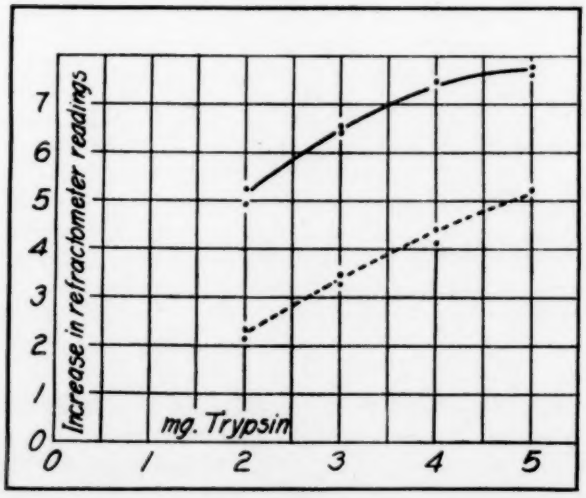

Chart 3.—The solid line indicates curve for milk which has been boiled for ten minutes; the broken line, that for certified milk not boiled. The time for digestion was four hours.

on it. But there seems to be no direct experimental evidence on this point. To confirm or refute the suggestion, the digestibility of raw and heat treated caseins was compared.

Casein for these studies was prepared from whole raw milk (often from skimmed milk) and from evaporated milk by precipitation in the iso-electric range for casein, using approximately molar lactic acid. Lactic acid was used in preference to acetic acid because the latter does not give as good coagulum with undiluted milk.[13] The acid was added drop by drop while the milk was vigorously agitated with a motor driven stirrer. Under these conditions a fine curd was obtained even from raw milk. The precipitated casein was separated from its whey by

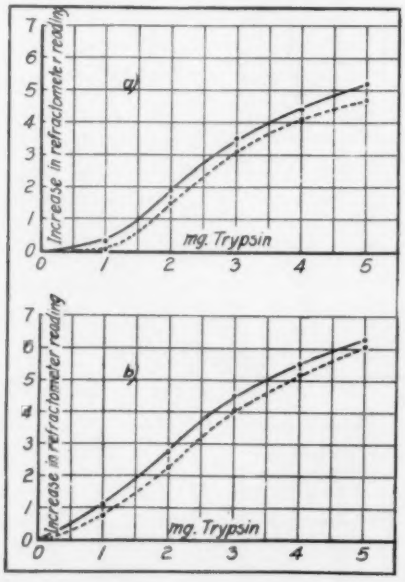
Increase in refractometer reading
a
mg. Trypsin
0 1 2 3 4 5
0 1 2 3 4 5 6 7
Increase in refractometer reading
b
mg. Trypsin
0 1 2 3 4 5
0 1 2 3 4 5 6 7

Chart 4.—The solid line indicates curve for pasteurized milk; the broken line, that for raw certified milk. *A* shows results for purchased milk; *B*, for certified milk pasteurized by holding at 60 degrees for thirty minutes. The time for digestion was four hours.

centrifuging. It was then washed ten or twelve times by suspension in water, until the washings were practically free from acid as determined by titration of the total washings. The washed casein was again suspended in water and was dissolved by addition of approximately 5 per cent sodium carbonate solution. This was added drop by drop with vigorous stirring of the casein suspension. In this way casein was readily dissolved without exceeding p_H 7.0. The casein solutions were

13. Tague, E. L.: Casein, Its Preparation, Chemistry and Technical Utilization, New York, Van Nostrand Company, 1926.

used for comparative study after their total nitrogen concentrations were adjusted to equal one another and so as to be approximately the same as that of whole milk. All digestions were made in solutions having an initial p_H of 8.2.

Chart 5 shows the results of an experiment in which the digestibility of a solution of casein preparation from evaporated milk was compared with that of a solution of casein from raw milk. Within the limits of experimental error, there is no demonstrable difference in digestibility. And, furthermore, the casein from raw milk digests more nearly like boiled or evaporated milk than like raw milk. However, it should be pointed out that although the "caseins" were prepared by identical procedures, they probably differ. This is so because the heat

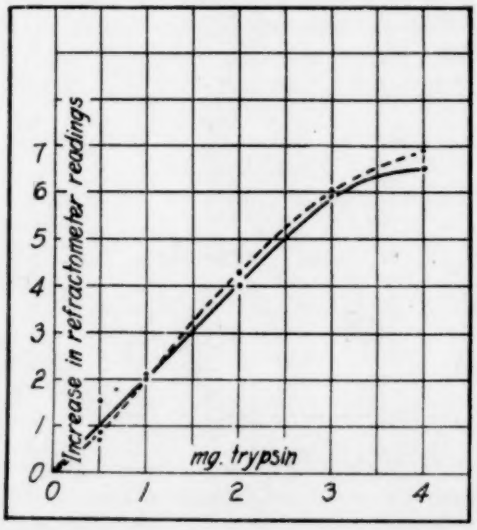

Chart 5.—Curves showing that the proteins precipitated from evaporated milk by lactic acid and thoroughly freed from whey were digested by trypsin, in vitro, at the same rate as the similarly prepared casein from raw milk. The solid line indicates results for casein from evaporated milk; the broken line, for that from raw certified milk. The total nitrogen concentration in each equaled 3.5 per cent protein. The time for digestion was four hours.

coagulated proteins of evaporated milk probably were present to contaminate the casein from evaporated milk. It is possible that a change in digestibility is here masked by the presence of the heat coagulable protein.

This objection was overcome by performing the same experiment with the following variation: casein from certified milk was prepared in the manner already described. The casein was then dissolved in a solution of sodium carbonate to give a solution of p_H 6.5, the p_H of fresh milk. This solution was divided into two equal portions one of

which was boiled for ten minutes. The experimental procedure from then on was exactly as in the previous experiment, and the result of digestion was exactly the same, that is, there was no difference in the rate of digestion of the raw and the heat treated casein. These results have been confirmed further by the use of casein prepared by other methods. Caseins prepared by precipitation with half saturated ammonium sulphate and subsequently dialyzed until sulphate-free, paracaseins from raw and evaporated milks prepared by rennin coagulation, and calcium caseinate, raw and boiled, all show the same thing. There is no difference in the digestibility of raw and heat treated casein by trypsin, and the digestion curves of casein resemble those of evaporated milk.

These results show that in heating no changes take place in the casein molecule which render it more digestible to trypsin. That no radical change takes place on heating casein is also indicated by the work of Cutler [14] using immunologic reactions. He stated that heat

TABLE 2.—*Differences in the Digestibility of Evaporated Milk Whey and Certified Milk Whey*

	Mg. Typsin	Mg. Nitrogen in 100 Cc. Filtrate	Increase in Soluble Nitrogen in Mg. per 100 Cc. Filtrate
Evaporated milk whey	0.0	21.45	0.0
	0.5	28.73	7.3
	1.0	31.47	10.0
	2.0	32.43	11.0
Certified milk whey	0.0	17.36	0.0
	0.5	18.26	0.9
	1.0	18.92	1.6
	2.0	31.86	14.5

applied to cow's milk in the process of preparing evaporated milk does not appear to change the antigenic capacity of the casein as determined by anaphylactic reactions.

THE CHANGE IN TRYPSIN DIGESTIBILITY IS DUE TO SOME HEAT-LABILE CONSTITUENT OF THE WHEY

These results have thrown suspicion on the whey. Lactic acid wheys, obtained in the course of casein precipitation from certified and evaporated milks were adjusted to p_H 8.2 and digested in the usual manner. When alkalinized, each whey gave a precipitate, but the amount of precipitate was noticeably more in the certified whey. This observation was confirmed by macro-Kjeldahl analyses which showed that the certified milk whey contained about twice as much total nitrogen as the other. The increase in soluble nitrogen (nitrogen not precipitated by trichloracetic acid) in these wheys as a result of digestion is shown in table 2

14. Cutler, O. I.: Antigenic Properties of Evaporated Milk, J. A. M. A. **92**:964 (March 23) 1929.

It must be borne in mind that these differences in digestibility are minimal, not maximal. This is due to the fact that the whey from certified milk contained about twice as much total nitrogen as that from evaporated milk. The experiment has been varied by comparing the digestibility of two portions of the same certified whey, one portion of which had been boiled ten minutes. The results were essentially the same. In the experiment, the results of which are given in detail in table 2, the lactate ion concentration may have been slightly different in the two wheys. In the second experiment referred to, there was no difference in the lactate concentration. Since the results of the two experiments are the same, the lactate ion concentration is probably not

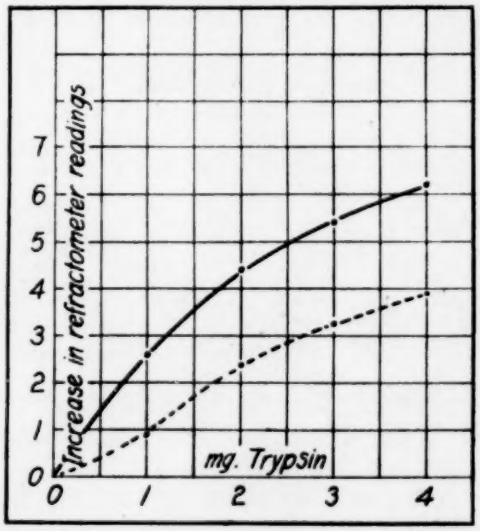

Chart 6.—The solid line indicates results for the digestion of a 3.3 per cent suspension of Hammarsten's casein in water. The initial p_H was 8.2 (no whey). The broken line indicates results for the digestion of a 3.3 per cent suspension of Hammarsten's casein in whey from certified milk. The caseins in this experiment were not so well dispersed into a colloidal state as in most other experiments.

a factor. Obviously, the factor which accounts for the difference in trypsin digestibility of raw and heated milks is in the wheys therefrom.

Further proof of this was obtained by suspending Hammarsten's casein in water and whey from certified milk, respectively, each adjusted to p_H 8.2. The digestion curves for this experiment (chart 6) show that there is something in the whey from certified milk which retards tryptic digestion. This inhibiting factor is heat labile. These observations again are in agreement with those of Cutler [14] who showed that there is an alteration in the antigenic properties of whey protein present

in raw milk when the milk is subjected to the heat necessary to evaporate and sterilize it in the process of manufacture of evaporated milk.

Söldner,[15] in 1888, first called attention to the fact that calcium and phosphorus are precipitated from milk in the ratio of 1 atom of calcium to 1 atom of phosphorus when milk is boiled, and that the amount precipitated varies with the amount and duration of the heat applied. Since the degree of change in the digestibility also appears to be a function of the amount and duration of heating, the question presents itself whether or not calcium and phosphate enter into the explanation of the altered digestibility of milk due to heat.

It seemed simplest to study the phosphate content of the lactic acid whey from certified milk before and after boiling the milk. To clarify the wheys, phosphate-free supercel (hy-flow) was used after it had first been ascertained that supercel does not adsorb phosphate. The method of phosphate analysis used was that of Fiske and Subbarow.[16] The results are listed in table 3. These results are calculated on the

TABLE 3.—*The Phosphate Content of Wheys from Certificate Milk Before and After Boiling the Milk*

Whey from Certified Milk: (Lactic Acid Precipitation)	From Raw Milk, Mg. per Cent	From Milk Boiled Ten Minutes, Mg. per Cent
Total phosphate in clarified whey	80.78	80.74
Total phosphate in trichloracetic acid filtrate	80.28	80.28
Inorganic phosphate in trichloracetic acid filtrate	63.52	64.59

basis of undiluted whey. That the results should be identical within the limits of experimental error seemed predictable from the histories of the wheys. Although the phosphate concentration is the same in the wheys from boiled and raw milks, the two wheys digested differently with trypsin, indicating that the phosphate concentration is not a determining factor.

Reasoning from the histories of the two wheys (the identical p_H at which they were prepared and the identical p_H to which they were alkalinized before digestion) it seemed unlikely that there could be any difference in the calcium concentration of the two. This, however, was not checked by actual experiment. In the calcium caseinate digestions already referred to, casein was prepared from raw milk in the usual manner except that it was finally dissolved in saturated calcium hydroxide in quantity just sufficient to replace the reported "nondiffusible" calcium of the milk. The p_H of this solution was exactly 7. After adjusting the p_H to that of fresh milk the solution was divided

15. Söldner, F.: Die Salze der Milch und ihre Beziehungen zu dem Verhalten des Kaseins, Landv. Versuchs. **35**:351, 1888.

16. Fiske, C. H., and Subbarow, Y.: The Colorimetric Determination of Phosphorus, J. Biol. Chem. **66**:375, 1925.

into two parts one of which was boiled ten minutes. The digestion curves of the raw and boiled calcium caseinates (chart 7) resemble the curves for boiled and evaporated whole milk. From this it again appears that calcium is probably not a factor in the digestibility differences under discussion and that the disturbing factor is in the whey.

This power which raw milk possesses of hindering the action of trypsin is not unique. Hahn,[17] in 1897, showed that normal blood serum possesses a marked resistance against the action of proteolytic enzymes, not being digested at all by dilutions of enzymes that will rapidly digest a serum which has been boiled. This work has been repeatedly confirmed. Wells [18] confirmed it by demonstrating a striking difference in the rate of autolysis of tissues kept in heated and unheated serums, using as his criterion the rate of disappearance of nuclear stain-

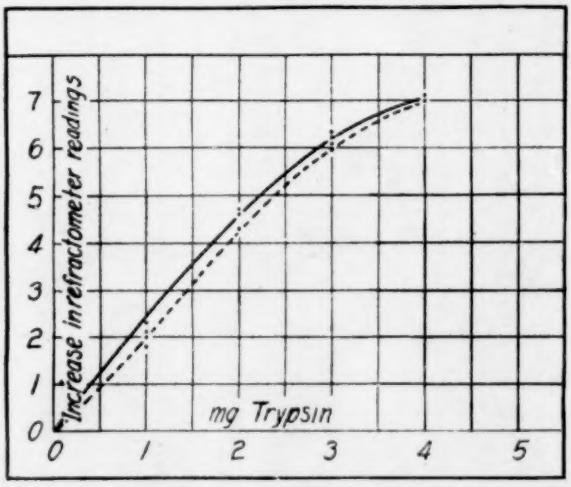

Chart 7.—The solid line indicates curve for calcium caseinate which has been boiled ten minutes; the broken line, that for the same calcium caseinate not boiled. The time for digestion was four hours.

ing. He ascribed the difference to the presence in normal serum of a thermolabile inhibiting substance or anti-enzyme. Efforts have been made by Landsteiner,[19] Glaessner [20] and by Cathcart,[21] to isolate the

17. Hahn, M.: Zur Kenntniss der Wirkungen des extravasculären Blutes, Klin. Wchnschr. **39**:499, 1897.

18. Wells, H. G.: The Relation of Autolysis to the Histological Changes Occurring in Necrotic Areas, J. M. Research **15**:149, 1906.

19. Landsteiner, K.: Zur Kenntniss der anti-fermentativen, lytischen und agglutinierenden Wirkungen des Blutserums und der Lymphe, Centralblt. f. Bakt. **27**:357, 1900.

20. Glaessner, K.: Ueber die antitryptische Wirkung des Blutes, Hofmeister Beiträge **4**:79, 1903.

21. Cathcart, E. P.: On the Antitryptic Action of Normal Serum, J. Physiol. **31**:497, 1904.

inhibiting substance. Landsteiner and Cathcart agree that the anti-action is found in connection with the albumin fraction. It may well be that in milk we are dealing with a similar, or even the same, "anti-trypsin" which exists in the serum of blood.

Returning to the data shown in table 2, it is important to note that the maximum inhibition of digestion in whey from certified milk takes place in those samples which have the least added trypsin. In fact, this is the relationship which was found in the initial portion of all curves when raw and evaporated milks were compared. The difference in the two curves is established in the course of the action of the first 1.5 to 2 mg. of trypsin; after more trypsin is added, the curves run

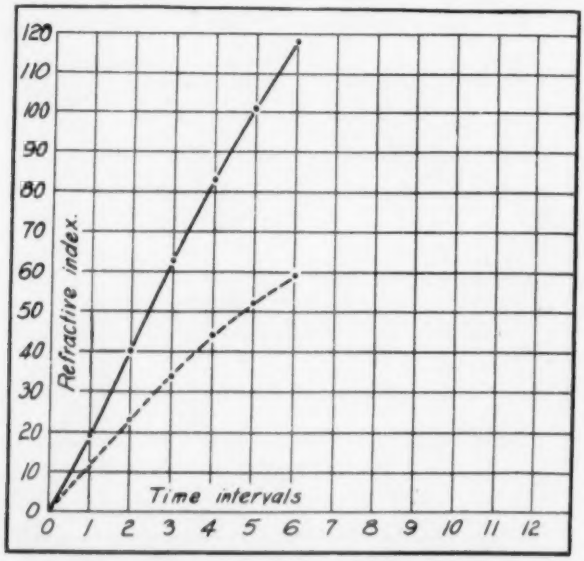

Chart 8.—The solid line indicates that no trypsin inhibitor is present; the broken line, that a trypsin inhibitor is present. The curves were plotted from data calculated on the basis of the following assumptions: that there are 100 molecules of casein and 20 of trypsin per unit volume, that the casein for the sake of convenience is a tetrapeptide, that the trypsin acts catalytically, that one mole of trypsin is decomposed every N minutes (broken curve) and that the refractive index is proportional to the molecular concentration.

parallel. The inference from this was that something other than casein was involved. That inference has been proved correct. With the concept of a tryptic inhibitor in mind it is easy to calculate what effect its presence or its absence should have on the tryptic digestion of casein if the following assumptions are made: 1. Casein is a polypeptide. 2. Trypsin acts catalytically. 3. The inhibiting substance reacts monomolecularly with trypsin rendering it inactive. 4. The refractive index

is proportional to molecular concentration. On these assumptions, data were calculated, and from these data the accompanying charts were drawn.

Chart 8 is based on the assumption that the trypsin concentration is constant and the time variable. Increases in molecular concentration are plotted as abscissae and time intervals as ordinates. This graph prompted the actual carrying out of an experiment in which raw and

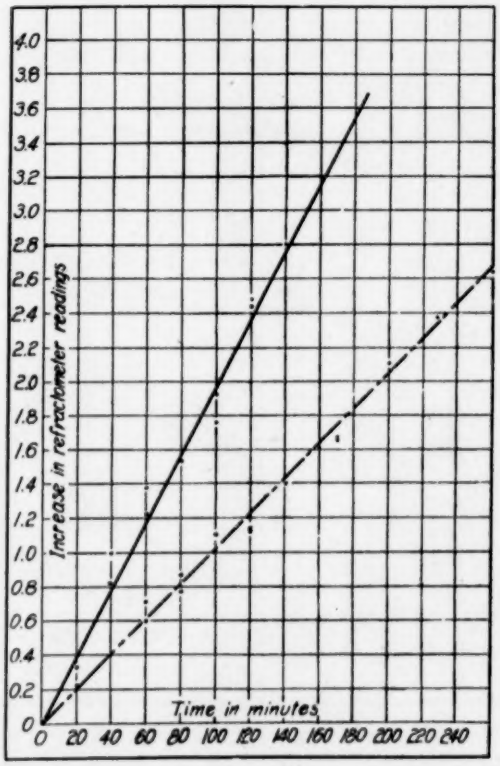

Chart 9.—The solid curve shows results for digestion of evaporated milk; the broken curve, for certified milk. The trypsin concentration is constant.

evaporated milks were digested with a constant quantity of trypsin and time as the variable. The results of this experiment are summarized in chart 9.

Chart 10 sums up the results of the theoretical calculations based on the assumption that trypsin is variable and time constant. These curves show a striking resemblance to the curves for the digestion of raw and evaporated milk. They are not offered as proof of the correctness of the suggestion that we are dealing with an antitrypsin but merely as circumstantial evidence that the antitrypsin hypothesis is not impossible.

THE QUESTION OF THE CURD IS STILL UNSOLVED

Before it can be stated definitely that differences in raw and heat treated milks exist other than those which involve the physical character of the curd, it must be shown what effect pepsin digestion has on the trypsin inhibitor, and the possibility of the presence of a pepsin inhibitor must also be investigated. Only when that is done will this work have practical significance. That work is under way. Probably the "anti-trypsin" destruction in heated milk is not of importance in making such milk better for infants. Very likely the most important factor resides in the peptic phase of digestion and thus probably particularly in the physical character of the curd.

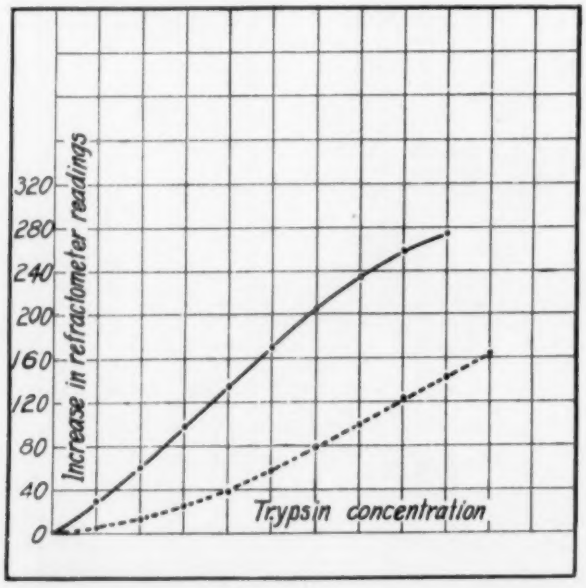

Chart 10.—The solid line indicates curve based on the following assumptions: 100 molecules of tetrapeptide, 10, 20, 20, 40, etc. moles of trypsin, no inhibiting substance and time constant. The broken line indicates curve based on the same assumptions with the addition of: 40 moles of inhibiting substance capable of reacting irreversibly with trypsin. The data in each case have been calculated to the end of 2N time interval so as to get the amino-acid effect on the curve.

SUMMARY

1. Raw milk when pasteurized, boiled or evaporated undergoes changes which make it more readily digested by trypsin in vitro than is raw milk. The changes are quantitatively greater for boiled and evaporated milk than for pasteurized milk.

2. The increase in trypsin digestibility appears to be a function of the temperature to which the milk is heated and the length of time it is heated.

3. The increase in trypsin digestibility is not correlated with a change in the buffer system of milk incidental to heating.

4. The increase in trypsin digestibility is not correlated with a change in the casein of the milk.

5. The change in trypsin digestibility is due to some heat-labile constituent of the whey. It is anticipated that this inhibitory substance will be found in the albumin portion of the whey. Calcium and phosphate are probably not involved.

6. It has been assumed that the tryptic inhibitor reacts monomolecularly with trypsin to inactivate it, and on this assumption theoretical curves have been calculated which show a marked resemblance to the curves obtained by actual experiment.

7. It is suggested that no practical significance can be attached to these results until the effect of peptic digestion as a precursor to tryptic digestion has been studied. The question whether the physical nature of the curd alone is responsible for the greater digestibility of heat treated milk in the stomach remains unanswered.

BLOOD TRANSFUSION IN DISEASES OF INFANTS AND CHILDREN *

L. KRAHULIK, M.D.
AND
L. A. KOCH, M.D.
BROOKLYN

In a study of 763 transfusions we have been impressed by the large number of conditions which were benefited by its use. We have classified these into four groups: (1) infections with secondary anemia, (2) nutritional disorders with and without infection, (3) diseases of the blood and (4) preoperative and postoperative conditions. The relative frequency of transfusions in each group is shown in table 1.

TABLE 1.—*General Classification*

Condition	Number of Cases	Number of Transfusions	Age		Vein Used		Donor			Reactions	
			Infants*	Children	Arm	Leg	Paternal	Maternal	Professional	Number	Per Cent
1. Infections with secondary anemia	253	481	143	110	464	17	234	55	192	57	12.0
2. Nutritional disorders	129	214	125	4	205	9	124	49	41	16	7.9
3. Diseases of the blood	23	48	16	7	43	5	23	10	15	1	2.1
4. Preoperative and postoperative conditions	12	20	12	...	20	..	11	3	6	1	5.0
Total	417	763	296	121	732	31	392	117	254	75	9.8

* Under 18 months of age.

Of the total number of patients who received transfusions, 253, or 60 per cent, had infection with secondary anemia. The cases of athrepsia and anhydremia with intoxication complicated by infection have been included under nutritional disorders. Sidbury [1] used transfusion for 298 patients with nutritional diseases, or 67 per cent of his total number. Only sixty-one patients, or 13 per cent of his total number, received transfusion for infection with secondary anemia. This variation is probably not due to a difference of opinion as to the indications but to the type of cases encountered in certain localities. The nutritional disorders for which we have used transfusion com-

* Submitted for publication, Aug. 21, 1929.

* From the Department of Pediatrics, the Long Island College Hospital.

* Read at a meeting of the Brooklyn Pediatric Society, Brooklyn, May 22, 1929.

1. Sidbury, J. B.: Transfusion in Infancy and Childhood, J. A. M. A. **89:** 855 (Sept. 10) 1927.

prised 31 per cent of our total number of cases, the diseases of the blood 6 per cent and the preoperative and postoperative conditions 3 per cent.

Table 2 shows in detail the diseases for which blood transfusion was used. The average duration of the illness before the first transfusion, the age of the patient, the average temperature and hemoglobin (Sahli) indicate the gravity of these conditions.

TABLE 2.—*Analysis of Cases of 417 Patients Treated by Transfusion*

Infections with secondary anemia:	Number of Cases	Number of Transfusions	Age: Infants	Age: Children	Average Duration Before Transfusion	Average Temperature, F.	Average Hemoglobin, per Cent*	Reactions: Number	Reactions: Per Cent	Mortality Rate: Died	Mortality Rate: Per Cent
Bronchopneumonia	73	118	60	13	10-16 da.	102-104	45-60	15	13	18	25
Lobar pneumonia	23	54	11	12	6-10 da.	101-104	45-55	8	15	3	13
Empyema	19	30	7	12	14-18 da.	101-103	40-55	5	17	4	21
Mastoiditis	50	108	26	24	14-21 da.	100-104	55-60	11	12	4	8
Lateral sinus phlebitis with septicemia	17	62	3	14	7-14 da.	101-104	45-55	12	19	6	35
Suppurative nephritis (pyelitis)	10	20	6	4	14-21 da.	101-103	45-60	..	..	4	40
Acute hemorrhagic nephritis	5	6	1	4	21 da.	99-101	50-60	1	17	1	20
Nephrosis	2	4	..	2	2-8 wk.	99	55	..	..	..	..
Carditis	9	15	1	8	6-12 mo.	99-101	30-45	1	7	2	22
Erysipelas	7	9	7	..	4-8 da.	102-104	50-60	..	..	6	85
Nutritional disorders:											
Athrepsia	30	53	30	..	1-3 mo.	99	60-75	2	4	9	30
Anhydremia with intoxication	79	127	77	2	1-7 da.	101	75-80	11	9	41	52
Celiac disease	4	7	2	2	2-14 mo.	98-100	50-65	..	..	1	25
Prematurity	11	18	11	..	10-20 da.	99	50-65	1	5	4	36
Diseases of the blood:											
Leukemia	4	17	3	1	2-7 mo.	102-104	40	..	..	4	100
Purpura hemorrhagica	2	4	..	2	4-7 da.	100	45-65	..	..	..	..
Hemorrhagic disease of the new-born											
infant	6	8	6	..	1-3 da.	100-101	30-50	..	..	2	33
Von Jaksch's anemia	9	14	7	2	3-8 mo.	99-101	25-35	1	11	..	..
Familial hemolytic icterus	1	1	..	1	1 yr.	101	33	..	..	..	..
Banti's disease	1	4	..	1	4 yr.	100	55	..	..	..	..
Preoperative and postoperative conditions:											
Pyloric stenosis	8	14	8	0	1-3 wk.	99-101	60-70	..	..	2	25
Intussusception	3	3	3	0	3-48 hr.	100-101	60-70	1	..	1	33
Miscellaneous	44	67	27	17	.....	.....	40-55	6	8.8	..	..

* Estimation by Sahli's method.

INFECTIONS WITH SECONDARY ANEMIA

Lobar Pneumonia and Bronchopneumonia.—We wish to call particular attention to the patients with pneumonia who received transfusion. This series includes seventy-three patients with bronchopneumonia and twenty-three with lobar pneumonia. Seventy-two of these were infants under 18 months of age. Eighty-eight, or 91 per cent, had some complication other than anemia. The most frequent complications were otitis media, mastoiditis, pleural effusion and pyuria. The average duration of the bronchopneumonia was from ten to sixteen days, and of the lobar pneumonia from six to ten days.

In practically all of these cases a severe anemia was encountered. Leake and Brown [2] have shown that in experimental pneumonia in dogs there was an appreciable decrease in the number of red blood cells without compensatory regeneration. The blood volume remained constant. Red blood cells were found to be destroyed in the capillary and tissue spaces of the lungs, liver, spleen and intestinal walls. Recently, Binger [3] called attention to the incomplete oxygenation of blood in pneumonia and its relief by oxygen therapy. Blood transfusion relieves this anemia and increases the number of available oxygen carriers. It is probable that serologic elements thus introduced are also instrumental in producing favorable results.

The patients without anemia usually recovered, and transfusion was not necessary. Transfusion of blood was not given until all other treatment had apparently failed, and often we felt that the measure had been delayed too long, i. e., given as a last resort. In several cases, transfusion through a vein of the leg was done while the patient was in the Roth-Barach oxygen hood. Occasionally two or three transfusions were given before improvement occurred. Some of the patients presented symptoms of circulatory collapse, but no ill effects were observed due to the administration of blood at such a time. Seventy-eight per cent of the cases were benefited and many terminated by crisis or lysis soon after transfusion. We find our experience corroborated in the literature. Bass,[4] in 1925, reported results obtained in ten cases similar to ours. He likewise felt that there was no danger in the administration of blood in these cases, even though some of the patients presented symptoms of circulatory collapse.

Our mortality rate in this group is 24.6 per cent in bronchopneumonia and 13 per cent in lobar pneumonia.

The abstracts of case reports and charts included are illustrations of the cases under discussion:

Case 1.—N. O., a girl, aged 4 years, was admitted to the hospital with bronchopneumonia of eleven days' duration. Her condition was critical. She was poorly nourished and markedly dehydrated. Cyanosis and dyspnea were extreme. She was having frequent convulsions. The hemoglobin taken before the administration of parenteral dextrose and physiologic solution of sodium chloride was 70 per cent. General improvement was noted after the first transfusion, and crisis occurred after the second.

Case 2.—A. T., a boy, aged 18 months, was admitted to the hospital with lobar pneumonia of six days' duration. On the twelfth day the hemoglobin was

2. Leake, C. D., and Brown, T. K.: The Loss of Circulating Erythrocytes in Certain Types of Experimental Pneumonia, J. Exper. Med. **36**:661 (Dec.) 1922.

3. Binger, C. A. L.: Anoxemia in Pneumonia and Its Relief by Oxygen Inhalation, J. Clin. Investigation **6**:203 (Oct.) 1928.

4. Bass, M. H.: The Association of Anemia and Pneumonia in Infants, Am. J. Dis. Child. **29**:318 (March) 1925.

48 per cent and his condition was critical. Transfusion on this day was followed by a rapid drop in temperature and recovery.

Empyema.—Nineteen patients who were admitted to the hospital with empyema were treated by transfusion and surgical drainage. Seven were infants and twelve were children. Severe anemia was a

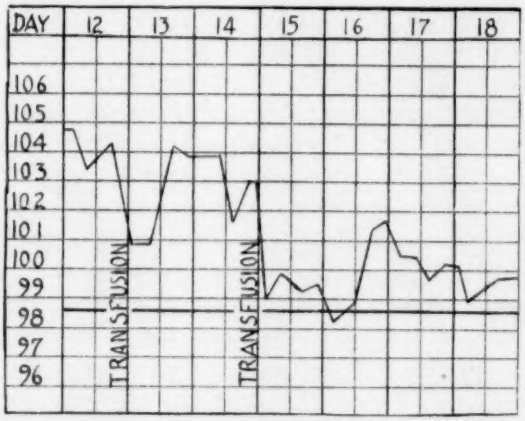

Chart 1.—Temperature chart of case 1; severe bronchopneumonia which improved after the first transfusion and terminated by crisis after the second.

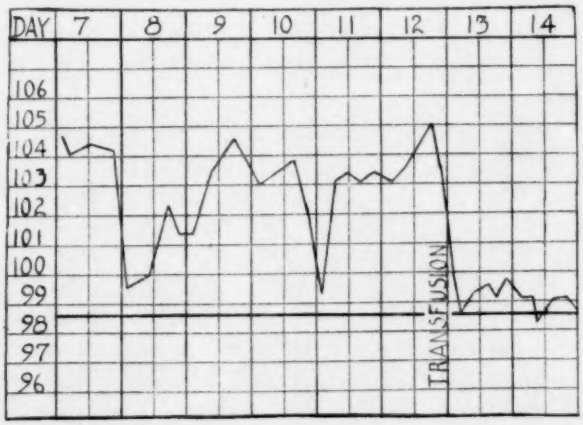

Chart 2.—Temperature chart of case 2; lobar pneumonia which terminated by crisis after transfusion on the twelfth day of the disease.

striking feature in this group. We attempted to keep the hemoglobin and red blood cells near a normal level by repeated transfusions. This procedure seemed to produce a general improvement and shortened what appeared to be an otherwise long and perhaps fatal illness. The mortality rate was 21 per cent.

Mastoiditis.—Fifty patients had mastoiditis; thirty-three of them had complications other than anemia. The most frequent complications were pyuria, cervical adenitis and streptodermatitis. Many of these patients were admitted to the hospital for otitis media and developed mastoiditis while in the hospital.

It was frequently observed that on admission the hemoglobin and red blood cells were only slightly diminished but as the infection extended a gradual or rapid drop was observed. Often the hemoglobin was lowered to 30 or 40 per cent. One could not expect these patients to react favorably to operation. Many patients with only mild anemia who were operated on for mastoiditis presented an unsatisfactory postoperative course. This was shown by a moderate elevation of temperature and discharge from the wound with no effort at repair. Following the administration of blood the temperature usually subsided and wound repair progressed satisfactorily. Keeping in mind the fact that in the milder cases transfusion was not necessary, one is impressed by the low mortality rate (8 per cent) in these, the more severe cases.

Nephritis.—We treated ten patients with suppurative nephritis (pyelitis) with transfusions. These patients had gross pus, a few red blood cells and albumin in the urine. The hemoglobin ranged from 45 to 60 per cent. The temperature was sustained between 101 and 103 F. Four of these patients received repeated transfusions with questionable benefit. In the others improvement was definite and permanent. In none of the cases did the urinalyses show improvement or the fever subside immediately after transfusion. The improvement was gradual.

The five patients with hemorrhagic nephritis were not seriously ill. The anemia due to loss of red blood cells in the urine was relieved by the administration of blood. All but one of these children recovered.

The two children with nephrosis had severe anemia. Soon after the administration of blood, favorable transitory effects were noted. The output of urine increased and the edema practically disappeared. One patient developed diarrhea, which was partly responsible for the decrease of the edema. We did not expect a permanent improvement from transfusion alone. Infected tonsils and adenoids were removed and infected paranasal sinuses were drained. One patient has been under observation for five years and leads a fairly active life. He has no edema but a small amount of albumin is present in the urine. The other patient was not followed.

Chronic Carditis.—The anemia in cases of severe carditis, especially in those of long standing, is particularly resistant to treatment with iron or liver. We have attempted to relieve this anemia by transfusion, knowing that the heart was seriously damaged and a cure could not be

expected. Nine patients received transfusion with at least temporary benefit. Two were done with the patient in a sitting posture. It was noted that during the procedure the pulse became slower and stronger but rose to its former level within a few hours. After transfusion, five of these patients ate better, began to gain weight and soon became ambulatory.

Erysipelas.—Seven infants with erysipelas received transfusion. We have not observed any curative effect. Although transfusion, the administration of erysipelas antitoxin and roentgen therapy were used, our mortality rate in this series was 85 per cent. A possible reason for the difference between our results and those reported by others is the fact that all of these patients were infants, most of them under the age of 1 year with a severe generalized type of infection. Three had positive blood cultures. We have not included in this group the cases of streptodermatitis which occurred as complications of postoperative mastoiditis.

THE NUTRITIONAL DISORDERS

Athrepsia.—Transfusions were administered to thirty infants with athrepsia. All were complicated by anemia, infection or both. Sixteen of these infants had unilateral or bilateral otitis media, four had pyuria, two had cervical adenitis and one had congenital syphilis. The hemoglobin ranged from 60 to 75 per cent.

These infants were fed whole lactic acid milk and dextrose corn syrup and received often as high as 200 calories per kilogram. Cod liver oil and orange juice were given in the usual quantity. Despite the regulation of the dietary, many failed to gain and some lost weight. Following transfusion, a marked improvement was frequently noted. A gain in weight, an increase in appetite and a more normal color resulted. However, in some of the infants no such reaction was encountered, and foci of infection had to be removed. In many of these cases operation on the mastoid and additional transfusions were necessary before improvement occurred. Our mortality rate in this group was 30 per cent.

Anhydremia with Intoxication.—Transfusion was used in the treatment of seventy-five patients who had anhydremia with intoxication. One hundred and twenty-seven transfusions were given. Forty-seven of the infants had unilateral or bilateral otitis media, three had bronchopneumonia, four had pyuria, two had paranasal sinusitis and nine had acute infection of the upper respiratory tract. In fourteen, we were unable to find any infection. The usual treatment was administration of physiologic solution of sodium chloride or Ringer's solution subcutaneously, dextrose (10 per cent) intravenously and transfusion. Fluid was administered every eight or twelve hours and if permanent

improvement did not occur, transfusion was repeated. Transfusions, although of little value when used alone, play an important part in the retention of body fluid in conjunction with the administration of physiologic solution of sodium chloride and dextrose solution. In many instances, removal of foci of infection was necessary, especially in the cases complicated by otitis media. Some cases responded to myringotomy. Antrotomy was necessary in twenty of our patients. Our mortality rate in these severe intoxications was 52 per cent.

Celiac Disease.—Four children with celiac disease were treated by transfusion in conjunction with a diet high in protein and low in fat and carbohydrate. Anemia was a complication in all of our cases. Sauer [5] reported twenty-five cases with good results from the three-phased protein diet. He called attention to the fact that one of his patients showed marked improvement in both appetite and weight following the intramuscular injection of 75 cc. of citrated blood. In ten of his cases the hemoglobin was less than 55 per cent, which is in accord with our cases. We observed an improvement in appetite and gain in weight after transfusion. One patient died of bronchopneumonia. The others are living and doing well.

Prematurity.—Eleven of our premature infants developed anemia, for which transfusion was given. The average hemoglobin was from 50 to 65 per cent. Hess [6] called attention to the fact that anemia develops quite regularly in the premature infant during the first three months of life. Seven of these infants were benefited. The anemia improved and a gain in weight occurred. Four did not respond. We feel that the procedure is of great benefit to this type of premature infant.

DISEASES OF THE BLOOD

The results obtained in the use of blood transfusion for various diseases of the blood do not differ from those already reported in the literature. In table 2 we have included nine cases of von Jaksch's anemia. All of these infants recovered. We wish to describe the cases classified as von Jaksch's anemia. The infants were anemic, rachitic, usually at or near normal weight, and had a greatly enlarged spleen and a moderately enlarged liver. The blood count showed a leukocytosis, with a relative increase in lymphocytes, diminished red blood cells and hemoglobin. Poikilocytosis, anisocytosis and nucleated red cells were present.

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5. Sauer, L. W.: Celiac Disease (Chronic Intestinal Indigestion): Etiology, Prognosis and Standardization of Treatment, Am. J. Dis. Child. **34**:934 (Dec.) 1927.

6. Hess, Julius H.: Feeding and the Nutritional Disorders of Infancy and Childhood, Philadelphia, F. A. Davis Company, 1928, p. 456.

PREOPERATIVE AND POSTOPERATIVE CONDITIONS

Eight infants with pyloric stenosis were prepared for operation by the administration of physiologic solution of sodium chloride and transfusion. These infants were malnourished, dehydrated and anemic. All but two required postoperative transfusion. Tisdall, Poole and Brown [7] used transfusion for preoperative and postoperative treatment in their cases of pyloric stenosis. They felt that it played a great part in reducing their mortality rate. Our mortality rate was 25 per cent.

SELECTION OF DONORS, METHODS, REACTIONS AND DOSAGE

Selection of Donors.—We have been extremely careful in selecting donors for transfusion. The health and general physical condition were always considered. One donor presented himself and when examined was found to have a severe chronic carditis and was promptly rejected. Donors who had given frequent transfusions and whose hemoglobin was less than 70 per cent were rejected. Fortunately, we have been able to use the father or mother in 66 per cent of our cases. In some instances, the parents were compatible but were rejected because of poor health. When both father and mother were compatible, the father was usually selected. The majority of the remaining 34 per cent were relatives. The true professional donor was not often used. Fasting donors were required, and no food was given the recipient four hours prior to transfusion.

Compatibility was determined by cross-matching and by hemolysis tests. In case neither parent nor available relatives were compatible, the patient was grouped and a donor of that group was obtained. He was likewise tested for compatibility. We have required that both sides of the test be compatible, that is, the recipient's cells and the donor's serum and the donor's cells and the recipient's serum must show no agglutination or hemolysis. Compatibility tests were performed before each transfusion even though the same donor was used. Astrowe [8] reported two cases in which prior to the first transfusion the bloods were compatible, but after a subsequent transfusion severe hemolysis occurred. Robertson and Rous [9] have shown experimentally in animals that following repeated transfusions from the same donor antibodies may develop and may cause hemolytic reactions. Wassermann tests were made on donors and recipients, and when an emergency arose and a Wassermann test could not be made, the Kahn test was substituted.

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7. Tisdall, F. F.; Poole, M. W., and Brown, A.: Pyloric Stenosis of Infants, Am. J. Dis. Child. **34**:180 (Aug.) 1927.

8. Astrowe, P. S.: Hemolysis Following Transfusion, J. A. M. A. **79**:1511, (Oct. 28) 1922.

9. Robertson, O. H., and Rous, P.: Sources of the Antibodies Developing After Repeated Transfusions, J. Exper. Med. **35**:141 (Feb.) 1922.

developed a peculiar erythematous rash resembling measles, which came on from six to eight days after transfusion and was accompanied by a mild febrile reaction. The rash disappeared after twenty-four hours, and no treatment was required.

Respiratory embarrassment, apparently due to too large a quantity of blood being transfused, occurred in eleven cases. The clinical manifestations of such a reaction are danger signals and transfusion should stop. A short hacking cough with restlessness and irritability are the first signs to appear. The patient who may have been asleep suddenly awakens and presents these symptoms. If more blood is introduced, cyanosis appears, and if the embarrassment is severe, respirations cease. The heart continues to beat. Artificial respiration with the administration of epinephrine has revived these patients. As a precautionary measure, epinephrine is always in readiness when a patient is receiving

TABLE 3.—*Amount of Blood Given for Various Weights*

Weight, Pounds	Average Amount Given, Cc.	Estimated Amount Using Rule, Cc.
5*	50 to 60	55*
10	100 to 120	100
15	130 to 150	136
20	150 to 175	167
25	175 to 200	192
30	200 to 225	214
50	250 to 300	275
75	300 to 350	322

* $\frac{5}{5 + 40} \times 500 = 55$ cc.

transfusion. This reaction was not due to incompatibility. These patients did not have a chill, although they usually developed a rise in temperature of 2 or 3 degrees. There was no hemoglobinuria or hematuria. We have been impressed by the seriousness of this type of reaction, and when the first symptoms appeared transfusion was immediately terminated.

It is particularly true that in order further to minimize reactions, the apparatus must be kept scrupulously clean. All tubing, adaptors, syringes and needles should be inspected before each transfusion. We have observed reactions (chills) due to blood which had accumulated around the small rings in the pistons.

In a total of 763 transfusions, 75, or 9.8 per cent, had reactions. The greatest percentage (12) of reactions occurred in patients with infection. Of these the highest percentage (19.3) occurred in the patients with lateral sinus phlebitis and septicemia. We feel that patients with septicemia and those with severe toxemia are most apt to have reactions.

Dosage.—The amount of blood given in this series has been carefully studied in relation to the weight of the patients. It has been

Methods.—The Unger method was used in nearly all cases. In a few cases in which only a small amount of blood was needed a three-way stopcock was used. We have found that for our purpose it is desirable to use the Unger method because of its simplicity, ease of operation and few resultant reactions. Often we wished to administer dextrose or physiologic solution of sodium chloride at the same time and found it convenient. It is true that an assistant is required, but any procedure as important as a transfusion should not be curtailed by the lack of help.

We have had no experience with intraperitoneal transfusions as advocated by Siperstein.[10] We have never used the longitudinal sinus for transfusion. The veins most frequently used were the median basilic at the elbow and the long saphenous at the ankle. The vein in the arm was most frequently employed (96 per cent). In infants it has often been necessary to expose a vein by a small longitudinal incision. The vein was never ligated, and in many cases the same vein was used two or three times. It is obvious that when administering a transfusion to a very sick infant if frequent attempts are made to enter veins in various parts of the body, considerable harm can be done. If, after a site is selected and the area is anesthetized the vein cannot be entered quickly, it should be exposed.

Reactions.—Reactions following transfusions are always undesirable. Even though the utmost care is used in the compatibility tests, proper selection and preparation of the donor, and proper administration of unmodified blood, a certain percentage of the cases will have reactions.

A post-transfusion rise in temperature of 1 F. or more, not explainable by some condition already present, constitutes a reaction. As a rule, no harm comes of a purely febrile reaction. By far the most severe reactions are manifested by a chill and rise in temperature. In some of our reactions with chills (2.5 per cent), the temperature rose to 105 or 106 F. The patients seemed to be in a critical state but all responded to heat and stimulation. There were no deaths. This type of reaction usually occurred about one hour after transfusion. In two cases hemoglobinuria was observed following a chill, and in one instance hemoglobin and red blood cells in large numbers were present in the urine.

Anaphylactic reactions occurred in four of our cases. All developed soon after transfusion. One patient developed a giant urticaria while the transfusion was being given, but no harmful results were encountered. Epinephrine was used for these cases. Two of our patients

10. Siperstein, D. M.: Intraperitoneal Transfusion with Citrated Blood, Am. J. Dis. Child. **25**:202 (March) 1923.

observed that infants will safely tolerate a relatively larger amount of blood than older children. Patients who were dehydrated could be given larger amounts than those with a normal blood volume. We have also noted that patients with severe anemia will not tolerate a larger amount than those who have a more normal hemoglobin. For this reason the degree of anemia as recommended by Halbertsma [11] was not used as a guide in determining the amount of blood to be given at one transfusion.

The average amount of blood that we have given for the various weights is shown in table 3. It has been found that these amounts can be closely computed by use of the principle of Young's rule for the dosage of drugs. If we consider the adult dose as 500 cc. and substitute weight in pounds for age in years and the constant denominator of 40 instead of 12, our rule will read:

$$\frac{\text{Weight}}{\text{weight} + 40} \times 500 = \text{amount to be given}$$

The application of this rule appears in table 3.

SUMMARY

1. Transfusion is of considerable value in the treatment for certain infections accompanied by secondary anemia.

2. Patients with lobar pneumonia and bronchopneumonia with anemia are definitely benefited by transfusion.

3. Blood transfusion used in the treatment for various nutritional disorders complicated by anemia is a most valuable therapeutic agent.

4. In the preoperative preparation of infants with pyloric stenosis the administration of transfusion and physiologic solution of sodium chloride is indispensable.

5. The proper selection of donors is of utmost importance in preparation for transfusion.

6. The method which permits the transfusion of unmodified whole blood without delay due to complicated apparatus is the method of choice.

7. Certain precautions must be taken to minimize reactions and ill effects from transfusions.

8. A simple rule, based on weight, for the computation of the amount of blood to be given at one transfusion is recommended.

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11. Halbertsma, T.: The Amount of Blood to be Transfused in Anemia of Children, Am. J. Dis. Child. **24**:269 (Oct.) 1922.

THE COMPARATIVE VALUE OF IRRADIATED ERGOSTEROL AND COD LIVER OIL AS A PROPHYLACTIC ANTIRACHITIC AGENT WHEN GIVEN IN EQUIVALENT DOSAGE ACCORDING TO RAT UNITS OF VITAMIN D*

D. J. BARNES, M.D.

M. J. BRADY, M.D.

AND

E. M. JAMES, M.S.

DETROIT

The use of cod liver oil as a prophylactic and therapeutic agent in the treatment of patients with rickets, while widespread and generally satisfactory, is being somewhat supplanted by irradiated ergosterol. It was felt desirable to study a controlled group of infants, some of whom were given cod liver oil, some irradiated ergosterol and others cod liver oil and irradiated ergosterol, keeping a number to whom no antirachitic agent was given.

A great many of the present observations on the therapeutic and prophylactic value of irradiated ergosterol are based on experiments on laboratory animals, and these reports are made still less accurate in that the dosage of irradiated ergosterol is stated in milligrams, though it is well known that different batches of irradiated ergosterol vary tremendously in the amount of vitamin D contained.

The only satisfactory way to make comparative evaluations of cod liver oil and irradiated ergosterol as antirachitic agents is to assay biologically the materials used and give like doses based on the number of rat units of vitamin D. Our materials were all assayed biologically according to Hawk and Bergein,[1] Steenback diet no. 2965 being used. A good grade of Norwegian cod liver oil was used and found to assay 3,750 rat units of vitamin D per ounce (30 cc.). The irradiated ergosterol was mixed with olive oil, tested in the same way and prepared to furnish 10,000 rat units of vitamin D per ounce (30 cc.). A combination of cod liver oil and irradiated ergosterol was prepared, enough irradiated ergosterol being added (6,250 rat units) to raise the rat unit value of the mixture to 10,000 rat units of vitamin D per ounce (30 cc.).

* Submitted for publication, Sept. 27, 1929.

* From the Child Welfare Division, Detroit Department of Health.

1. Hawk and Bergein: Practical Physiological Chemistry, ed. 9, Philadelphia, P. Blakiston's Son & Company, 1926, p. 835.

Howland and Kramer's [2] method of taking the calcium times the phosphorus and considering all cases with a product of 40 or more as normal was used in separating the rachitic from the normal infants. The normal blood calcium was found to vary from 9.4 to 12.2 mg. per hundred cubic centimeters, while the normal blood phosphorus varied from 4.4 to 6.6 mg. per hundred cubic centimeters.

A safe middle ground for dosage was sought, and, in accordance with the suggestion of Eliot,[3] 3 teaspoonfuls of cod liver oil per day were used. From our data it was possible to judge the contention of Hess [4] that many infants require from 7 to 8 teaspoonfuls of cod liver oil daily, as well as to compare the relative merit of like doses of cod liver oil, irradiated ergosterol and a combination of cod liver oil plus irradiated ergosterol as prophylactic antirachitic agents.

No attempt was made to select the infants. They were taken as they came into the clinic and put in rotation in one of the four groups. More than 100 cases were dropped during the experiment which started in December, 1928, and the material which comprises this report was taken from a study completed in April, 1929, of the remaining 216 cases. Determinations on the blood calcium and phosphorus were made with the Tweedy [5] modification of the Kramer and Tisdall method for the former and the modified Fiske and Subbarrow [6] method for the latter. Roentgen examinations of the long bones were made, and the results are reported at this time merely as a check on the blood chemistry. A separate correlation study of the blood chemistry and the roentgen observations is being made. The infants were all weighed and examined regularly, and received adequate diets. A few of the subjects were found to be rachitic at the start but were carried in their respective groups, with the exception of two control cases, in which the subjects developed severe intercurrent infections. For fear of jeopardizing their lives these subjects were taken from this series, given cod liver oil and removed from the experiment.

The criticism may be made that in such a group as is represented here direct control of the patient is lost. It was felt that with the bimonthly visits at the clinic and the bimonthly home visits made by the Child Welfare nurses such a factor would be inconsequential, and that since this same error was necessarily operative through all groups

2. Howland, J., and Kramer, B.: Factors Concerned in the Calcification of Bone, Tr. Am. Pediat. Soc. **34**:204, 1922.

3. Eliot, M. M.: The Control of Rickets, J. A. M. A. **85**:653 (Aug. 29) 1925.

4. Hess, A. F., and Lewis, J. M.: Clinical Experience with Irradiated Ergosterol, J. A. M. A. **91**:783 (Sept. 15) 1928.

5. Tweedy, W. R., and Koch, F. C.: Suggested Modification of Kramer-Tisdall Method, J. Lab. & Clin. Med. **14**:747, 1929.

6. Fiske, C. H., and Subbarow, Y.: J. Biol. Chem. **66**:375, 1925.

it would not vitiate the results. On the other hand, this study represents observations on infants cared for in homes and hence under more nearly normal conditions than would be found in an institution.

Table 1 represents the results in a group of 57 infants given daily 1,250 rat units of vitamin D in the form of irradiated ergosterol studied according to age, sex, color, weight and diet, that is, whether breast-fed or formula-fed. The average initial blood calcium was 9.4 mg. per hundred cubic centimeters; the blood phosphorus, 5.3 mg. per hundred cubic centimeters and the calcium-phosphorus product, 50.2. The final average blood calcium was 9.5 mg. per hundred cubic centimeters; the blood phosphorus was 4.1 mg. per hundred cubic centimeters, and the calcium-phophorus product was 39.9. The average gain in weight was 2.7 pounds, and the average initial age was 5.6 months. There were 32 male, 25 female, 45 colored, 12 white, 32 breast-fed and 25 formula-fed infants in the group (table 5).

Table 2 shows the results in a study of a group of 64 infants who were given daily 3 teaspoonfuls (1,400 rat units of vitamin D) of cod liver oil. They were observed according to age, sex, color, weight and type of feeding. There were 36 male, 28 female, 44 colored, 20 white, 37 breast-fed and 27 formula-fed infants (table 5). The average gain in weight was 3 pounds, and the average age was 6.9 months at the beginning of the experiment. The average initial blood calcium was 9.4 mg. per hundred cubic centimeters; the blood phosphorus was 5.5 mg. per hundred cubic centimeters, and the calcium-phosphorus product was 51.6. At the end of the experiment the average blood calcium was 10.7 mg. per hundred cubic centimeters; the blood phosphorus, 5.2 mg. per hundred cubic centimeters, and the calcium-phosphorus product, 56.8.

Table 3 represents the observations on 49 infants who were given daily 3 teaspoonfuls of a mixture of cod liver oil and irradiated ergosterol representing a total daily dosage of 3,750 rat units of vitamin D. They were studied according to age, sex, color, weight and type of feeding, that is, breast-fed or formula-fed. There were 32 male, 17 female, 33 colored, 16 white, 23 breast-fed and 26 formula-fed infants in this group (table 5). The average gain in weight was 3.1 pounds, and the average initial age was 5.7 months. The initial average blood calcium was 9.6 mg. per hundred cubic centimeters; the blood phosphorus, 5.9 mg. per hundred cubic centimeters, and the calcium-phosphorus product, 56.9. The final average blood calcium was 10.6 mg. per hundred cubic centimeters; the blood phosphorus was 5.43 mg. per hundred cubic centimeters, and the calcium-phosphorus product was 57.4.

Table 4 shows the results in a control group of 46 infants who received no antirachitic agent. They were similarly observed according to age,

TABLE 1.—*The Effect on Infants of Irradiated Ergosterol in a Daily Dosage of 1,250 Rat Units of Vitamin D* *

Number	Age	Duration in Days	Sex	Race	Diet	Initial					Final					Comment
						Weight	Calcium	Phosphorus	Ca × P	Roentgen Observations	Weight	Calcium	Phosphorus	Ca × P	Roentgen Observations	
913	12	94	F	W	F+V	16.4	7.4	3.9	28.9	+	17.7	11.6	5.3	61.5	—	1/8/29, slight acute bronchitis and recovery
948	2	110	M	C	B+F	10.2	9.5	5.7	54.1	—	14.0	10.7	5.0	53.5	—	
1064	5	111	F	C	B+C	12.8	8.0	7.5	60.0	+	14.6	10.3	1.7	17.5	+	
892	3	96	F	C	B	8.8	10.6	7.0	74.2		11.1	9.8	3.2	31.4		
1025	6	105	F	C	B+F	13.1	6.7	3.0	20.1	+	14.0	6.0	2.1	12.6	+	
1001	13	98	M	W	F+C+V	23.6	10.5	6.1	64.0	—	25.8	10.1	4.1	41.4	—	
937	12	110	F	C	F+C+V	20.6	10.0	7.0	70.0	—	22.9	10.5	4.7	49.3	—	
1041	8	105	M	C	F	17.7	8.5	4.5	38.2		20.2	9.7	5.1	49.5		
201	8	87	M	W	B	20.7	9.9	5.4	53.5	—	22.0	9.8	4.0	39.2	—	
1077	12	84	M	C	F+C+V	22.2	9.8	5.3	51.9	—	24.5	10.0	5.4	54.0	—	
193	10	92	M	C	F+C	17.5	9.8	5.6	54.9	—	19.0	10.2	5.1	52.0	—	Acute bronchitis, 2/20/29
212	3	...	F	W	F	9.7	9.2	6.6	60.7		14.2	9.6	5.4	51.8		
967	45	107	M	C	F+C	15.2	8.8	4.9	43.1	—	17.2	9.5	2.5	22.7	+	
989	11	90	M	C	F+C+V	19.7	10.4	6.7	69.7	—	20.6	9.0	2.5	22.5	—	
315	6	84	M	C	B+F	18.4	9.0	4.4	39.6	—	19.2	10.1	4.9	49.5	—	
174	10	119	F	C	F	19.4	10.4	7.1	73.8	—	22.7	9.2	4.3	39.6	—	
901	3	112	F	C	B+C	14.4	9.1	4.1	37.3		16.6	8.2	3.2	26.2		
1023	3	91	F	C	B	13.5	10.0	4.7	47.0	+	14.4	9.6	2.8	26.9	+	
897	4	110	F	C	B	10.6	8.0	4.2	33.6	—	13.8	9.2	2.7	24.8		
955	8	98	M	C	F+C	20.5	9.2	5.5	50.6	—	22.6	10.2	5.5	56.1	—	
249	7	79	F	C	F+C+V	17.9	8.5	2.6	22.1	—	19.7	8.8	5.6	49.3	—	
974	4	84	F	C	B	12.8	9.5	4.7	44.6	—	18.8	8.2	3.8	31.2	+	Intercurrent and acute otitis media
209	5	113	F	C	B	13.7	9.3	4.4	40.9		16.6	10.4	3.5	36.4		
986	12	94	F	C	F+C+V	19.5	9.7	3.7	35.9	—	20.9	10.9	2.4	26.2	—	
959	1.7	104	M	C	B+F	11.1	10.1	6.1	61.6	—	15.0	10.0	5.1	51.0	—	
911	11	94	F	W	F+C+V	12.8	9.4	2.8	26.3	+	13.8	9.6	2.5	24.0	+	
921	11	94	M	W	F+C+V	13.5	9.4	2.8	26.3	+	14.3	8.8	2.6	22.9	—	

980	2	86	M	C	B	11.8	7.4	5.4	40.0	—	14.1	9.7	2.8	27.2	+	
982	1	87	M	C	B	9.5	10.5	4.9	51.4	—	15.0	10.5	3.2	33.6	+	
251	6	103	M	W	F+C+V	14.2	10.0	5.3	53.0	—	17.1	11.8	6.3	74.3	—	
956	8	106	M	C	B+C+V	18.2	9.8	6.1	59.8		20.7	4.7	5.1	24.0	—	
244	6	83	M	W	B	15.0	9.9	4.8	47.5	—	17.2	9.7	5.9	57.2	—	Congenital syphilis
1067	3	100	M	C	B	13.8	8.2	4.6	37.7	+	15.8	9.5	2.5	24.7	+	
316	1	91	M	C	B	10.6	9.8	5.8	56.8	—	14.8	9.9	3.1	30.7	+	
458	3	92	F	C	B+C	12.1	9.4	5.6	52.6	—	17.1	10.6	3.9	41.3	—	
1073	8	99	M	C	F+C+V	16.3	8.9	6.3	56.1	—	17.9	9.4	3.3	31.0	—	
442	5	79	M	C	F+C	15.5	10.4	6.8	70.7	—	17.9	10.6	8.8	93.3	—	
1046	7	101	M	C	F	16.9	4.5	3.3	14.9	+	18.4	9.4	3.3	31.0	+	
1024	4	96	F	C	B+F	13.7	10.3	5.2	53.6	—	15.6	10.5	4.0	42.0	—	
318	7	87	M	C	B+F	17.5	9.7	5.6	54.3	+	18.6	9.6	2.8	26.9	+	
988	1	87	M	C	B	8.6	9.6	2.4	23.0	—	14.6	9.6	4.7	45.1	—	
981	2	95	M	C	B+F	9.5	8.2	4.7	38.5		13.5	7.4	4.5	33.3	+	
940	1.7	114	M	C	B	11.0	8.0	6.0	48.0	±	14.8	6.1	4.1	25.0		
900	9	104	F	C	F	17.8	10.4	6.3	65.5	—	19.6	10.4	5.1	53.0	—	
1016	5	96	F	C	F	12.6	11.2	6.6	73.9	—	15.8	10.1	5.8	58.6	—	
1022	1	105	M	C	B+C	9.4	9.8	5.7	55.9	—	14.1	7.0	3.5	24.5	+	
883	2	108	F	C	B	10.3	10.8	6.5	70.2		13.7	10.2	6.4	65.3		
171	8	102	F	W	F+C+V	15.9	9.9	6.3	62.4	—	17.5	11.3	5.0	56.5	—	
882	5	105	F	C	F+C	12.6	10.5	6.1	64.0		14.6	11.6	5.6	65.0		
899	3.5	105	F	W	F	14.1	9.9	6.5	64.3		17.9	9.0	4.0	36.0		
898	4.5	108	F	C	B	15.4	8.9	5.7	50.7		18.1	7.0	3.8	26.6		
969	0.8	110	M	C	B+F	8.0	9.0	6.5	59.5	—	14.3	10.0	2.9	29.0	+	
222	5	79	M	C	B	16.1	10.3	4.2	43.3	+	17.0	8.8	3.0	26.4	+	
962	4	105	M	C	B	15.8	7.9	5.2	41.1	—	17.2	8.1	3.6	29.2	+	
932	10	91	M	W	F+C+V	19.2	10.3	5.7	58.7	—	21.7	9.9	5.2	51.5	—	
161	1	94	M	C	B+F	9.7	8.8	5.6	49.3	—	15.0	9.2	3.0	27.6	+	
894	2	101	F	W	B	8.6	10.2	5.9	60.2		13.2	10.8	5.4	58.3		
Average.....		98	..	..	.....	14.5	9.36	5.3	50.2		17.2	9.51	4.13	39.9		

* In this and the accompanying tables the following are used: Age—expressed in months or fraction thereof. Sex—M, male; F, female. Race—C, colored; W, caucasian. Diet—B, breast-fed; F, formula-fed; V, vegetables; C, cereal. Weight—expressed in pounds or fraction thereof. Calcium and phosphorus—expressed in milligrams per cubic centimeter. Roentgen observations—definite evidence of rickets +; no evidence of rickets —.

TABLE 2.—*The Effect on Infants of Three Teaspoonfuls of Cod Liver Oil (1,400 Rat Units of Vitamin D) Daily from December, 1928, to April, 1929*

Number	Age	Duration in Days	Sex	Race	Diet	Initial					Final					Comment
						Weight	Calcium	Phosphorus	Ca × P	Roentgen Observations	Weight	Calcium	Phosphorus	Ca × P	Roentgen Observations	
213	13	81	F	W	F+C+V	19.9	9.5	6.5	61.7	—	21.1	10.5	6.6	69.3	—	
910	11	83	M	W	B+F	14.1	9.9	2.2	21.8		13.6	12.5	4.8	60.0		
929	11	90	M	W	B+F	15.4	9.8	2.1	20.6		16.2	10.1	3.9	39.4		Mastoiditis during treatment
946	6	105	F	W	F+C+V	14.7	9.0	4.7	42.3	—	17.4	10.4	5.1	53.0	—	
100	8	78	M	W	B	17.1	7.8	4.3	33.5	+	17.2	9.4	5.9	55.5	—	Bronchopneumonia with recovery in March
1070	5	82	F	C	B	15.3	7.9	5.9	46.6	—	17.2	11.5	6.0	69.0	—	
965	4.5	105	F	C	B+F	14.6	9.7	6.2	60.1	—	20.0	....	5.5	....	—	
127	4	124	M	C	B	17.2	6.4	3.4	21.8	—	19.7	10.3	4.9	50.5	—	
455	10	93	F	C	F+C+V	17.9	10.2	5.7	58.1	—	19.0	11.7	5.5	64.4	—	
452	10	93	M	C	F+C+V	18.6	8.6	5.7	49.0	—	19.6	11.7	5.6	65.5	—	
152	10	111	M	C	F+C+V	19.3	10.6	5.9	62.5	—	19.5	11.4	5.1	58.1	—	
1075	10	84	M	C	F+C+V	20.6	10.1	5.3	53.5	—	22.4	10.1	4.9	49.5	—	
163	6	84	M	W	F	17.7	10.4	5.7	59.3	—	19.2	9.8	5.7	55.9	—	
979	4	96	M	C	B+F	16.3	7.1	4.7	33.4		20.1	10.5	4.4	46.2		
187	5	92	F	C	B+C	18.2	7.0	5.0	35.0	+	20.4	10.3	3.8	39.1	—	Overweight
271	4	107	F	C	B+F	12.0	9.9	5.2	51.5	—	14.7	10.9	5.2	56.6	—	
998	8	96	F	C	F+C	16.9	9.7	6.1	59.2	—	18.9	10.7	5.6	59.9	—	
196	4	111	F	C	B	16.3	10.0	6.5	65.0	—	20.4	12.2	5.7	69.5	—	
135	11	111	M	W	F+C+V	17.9	10.6	6.7	71.0	—	19.2	11.2	5.0	56.0	—	
275	1.7	104	M	C	B	9.5	10.0	5.4	54.0	—	13.1	10.4	4.5	46.8	—	
270	2	104	F	C	B	9.1	8.2	5.4	44.3	—	12.7	....	4.1	....	—	
923	11	79	F	C	B+C+V	18.2	9.4	4.8	45.1	—	19.3	10.2	4.4	44.9	—	
903	4.5	86	F	C	B+F	11.2	10.1	5.2	52.5	—	15.2	11.1	5.7	63.3	—	
276	10	117	M	W	C+V	17.5	6.8	3.1	21.1	+	22.3	11.0	4.9	53.9	—	
246	8	84	M	W	B+F	17.4	9.6	4.6	44.2	—	18.6	10.7	5.8	62.1	—	
272	10	117	M	C	F+C+V	19.8	10.2	4.6	46.9	—	25.0	10.8	6.7	72.4	—	
196	4.5	99	F	W	B	14.6	9.4	5.4	50.8	—	17.4	10.0	5.5	55.0	—	
110	12.5	134	F	C	F+C+V	16.7	9.8	5.8	56.8	—	17.2	11.2	5.0	56.0	—	
944	2	107	F	C	B	14.1	8.7	5.7	49.6	+	20.1	11.2	5.2	58.2	—	

1039	9	80	F	C	F+C+V	17.0	9.7	5.8	56.3	—	19.6	10.5	4.7	49.3	—	
1009	4	93	M	C	B+C	16.6	9.8	5.4	52.9	—	19.7	11.4	5.3	60.4	—	
970	11	115	F	C	F+C+V	17.2	10.2	6.6	68.0	—	19.8	9.9	5.6	55.4	—	
1065	3	96	F	C	B+F	13.2	9.9	7.3	72.3	—	17.9	10.1	5.2	52.5	—	
908	8	108	F	C	B+C+V	17.6	9.6	6.6	68.4	—	18.6	10.8	4.2	43.3	—	
145	7	103	M	W	F+C+V	16.0	9.5	5.0	47.5	—	20.1	9.7	4.6	44.6	—	
146	7	103	M	W	F+C+V	13.2	9.7	5.0	48.5	—	17.5	10.4	5.2	54.1	—	
988	13	114	M	C	F+C+V	20.9	9.1	5.5	50.0	+	23.2	10.0	4.0	40.0	—	
211	13	85	M	W	C+V	22.4	10.2	6.0	61.2		24.1	10.7	5.0	53.5		
259	4	115	M	C	B	13.6	8.6	4.5	38.7	+	18.6	11.1	4.5	50.0	—	
241	0.8	85	F	W	B+F	6.6	9.9	6.3	62.4		11.2	10.0	5.7	57.0		
885	13	102	M	C	F+C+V	25.1	10.0	5.8	58.0		27.0	10.4	5.1	53.0		
139	8	114	F	W	B	18.4	10.2	6.7	68.3	—	21.1	10.8	4.7	50.8	—	
985	8	102	M	C	B	18.7	8.8	4.8	42.2	—	21.9	10.5	5.6	58.8	—	
958	1.2	98	M	C	B	8.7	9.2	5.0	46.0		14.4	10.0	4.8	48.0	+	
987	7	86	M	C	B	15.7	10.2	4.6	46.9	+	17.6	10.9	6.8	74.1	—	
143	11	109	F	W	B+F+C+V	18.2	9.3	5.3	49.3	—	19.0	10.7	5.4	57.8	—	
144	6	110	M	W	B	16.1	11.3	5.7	64.4	—	20.0	11.6	6.6	76.6	—	
200	12	84	F	W	F+C+V	20.7	9.9	5.6	55.4	—	22.1	10.6	6.9	73.1	—	
115	5	122	M	C	F+C	16.6	5.7	6.4	36.5	+	18.2	9.7	3.5	34.0	+	Noncooperative
960	13	75	F	C	F+C+V	18.3	8.9	5.8	51.6	—	19.8	10.5	5.3	55.6	—	
935	8.5	86	F	C	F+C+V	16.3	10.6	6.3	66.8	—	18.5	11.6	5.9	68.4	—	
1040	2	106	M	C	B+F	8.1	9.3	5.2	48.4		11.9	11.5	5.3	60.9	—	
274	2.5	107	M	C	B	9.7	8.1	4.0	32.4		14.4	10.5	4.4	46.2	—	
105	9	118	F	C	B+C+V	14.8	10.3	4.7	48.4	+	17.2	9.9	5.4	53.5	—	
268	5	102	M	C	B+F	13.0	10.1	5.3	53.5	—	15.1	9.6	5.0	48.0	—	
128	1	110	F	C	F	8.1	9.4	7.9	74.3	—	13.6	9.9	6.0	59.4	—	
941	9	120	M	C	F+C+V	22.1	8.9	6.7	59.6		25.6	10.8	6.0	64.8		
258	11	117	M	C	F+C+V	22.7	10.2	5.9	60.2	—	24.7	10.7	7.1	76.0	—	
102	3	124	M	W	B	12.8	10.0	5.4	54.0		17.2	12.7	5.5	69.8	—	
129	1	126	M	C	B+F	6.6	....	...	....	+	14.5	10.9	6.3	68.7	—	
1066	1	98	M	C	B+F	8.0	9.7	6.5	63.0	—	12.4	11.1	5.6	62.2	—	One-half teaspoonful cod liver oil three times a day
116	1.5	121	M	C	B	8.7	10.2	6.5	66.3	—	14.5	10.6	6.2	65.7	—	
200	1	115	F	C	B	9.0	9.3	6.5	60.4	—	14.6	11.9	4.7	55.9	—	
1007	12	98	M	W	C+V	17.1	9.0	6.0	54.0		20.0	10.7	5.0	53.5	—	
Average.....		101	..	..	.....	15.5	9.38	5.47	51.6		18.5	10.7	5.19	56.8		

TABLE 3.—*The Effect on Infants of Cod Liver Oil and Irradiated Ergosterol Given in Dosage of Three Teaspoonfuls a Day (3,750 Rat Units of Vitamin D)*

Number	Age	Duration in Days	Sex	Race	Diet	Initial				Roentgen Observations	Final				Roentgen Observations	Comment
						Weight	Calcium	Phosphorus	Ca × P		Weight	Calcium	Phosphorus	Ca × P		
888	4.5	102	F	C	B+C	14.5	10.6	4.3	45.6	—	17.3	10.6	3.7	39.2	—	
191	9	100	M	C	F+C+V	16.6	9.1	7.4	67.3	—	18.2	10.5	5.5	57.8	—	
1008	11	91	F	W	F+C+V	15.7	10.6	6.4	67.8	—	16.5	9.9	4.7	46.5	—	
190	1	96	M	C	B	10.4	7.2	5.1	36.7	—	15.8	11.6	4.4	51.0	—	
1042	3	111	M	W	F	11.0	9.7	6.6	64.0		17.9	10.8	7.0	75.6	—	1/29/29, thrush
1035	9	91	F	C	F+C+V	16.2	10.3	5.2	53.6	—	17.0	10.9	4.4	48.0	—	
225	3	80	M	C	B	15.4	10.0	6.3	63.0	—	20.4	10.5	4.2	44.1	—	
1060	1.2	115	M	C	F	10.3	9.9	6.5	64.4	—	14.7	10.3	5.0	51.5	—	
114	5	117	F	O	F+C+V	10.6	12.9	6.1	78.7	+	17.2	10.5	4.7	49.3	—	
219	3	87	F	O	F	11.9	10.2	6.9	70.4	—	14.6	10.2	6.1	62.2	—	
141	6	106	F	W	B+F	14.2	11.0	6.8	74.8	—	16.2	9.2	5.8	53.4	—	
1078	4	104	F	W	F	13.3	9.5	7.2	68.4	—	16.2	9.9	6.3	62.4	—	
140	3	105	M	W	F	11.3	10.7	7.1	76.0	+	14.0	10.2	5.4	55.1	—	
263	1	110	M	C	B	10.7	6.4	5.0	32.0		14.1	11.2	7.2	80.6	—	
214	12	89	M	W	F	19.0	9.9	5.5	54.5	—	19.8	10.9	4.8	52.3	—	
999	9	105	M	C	F	17.5	7.3	4.4	32.1	+	18.7	10.1	5.2	52.5	—	
994	2	91	M	C	B	11.4	9.8	4.9	48.0	—	16.1	10.3	5.3	54.6	—	
1049	4.5	112	M	C	F	14.6	9.2	6.9	63.5	—	19.4	11.7	7.1	83.1	—	
1003	2	92	M	C	B+F	11.0	10.3	6.1	62.8	—	12.1	10.1	5.9	59.6	—	
983	14	92	F	C	F+C+V	18.9	10.0	6.1	61.0	—	20.0	10.7	5.9	63.1	—	
100	13	130	M	C	F+C+V	23.4	9.7	6.7	65.0	—	25.6	10.5	5.6	58.8	—	
265	8	104	F	C	F+C+V	18.4	10.8	7.1	76.7	—	21.4	11.6	5.8	67.3	—	
934	4	87	M	W	F	9.1	7.5	5.2	39.0	—	13.2	12.0	5.6	67.2	—	
109	8	131	F	C	F+C+V	14.1	10.0	7.1	71.0	—	17.9	11.0	5.7	62.7	—	
1015	6	95	M	C	F	15.5	9.7	5.0	48.5	—	16.9	10.1	4.9	49.5	—	
1036	3	103	F	C	B	9.7	8.3	4.9	40.7	—	12.5	10.7	3.9	41.7	—	
950	4	106	M	C	B+F	14.0	9.3	6.0	55.8	—	21.2	10.3	6.5	67.0	—	
984	7	84	M	C	B+D+V	18.8	10.2	5.3	54.1	—	19.5	10.7	5.6	59.9	—	
147	4.5	104	F	W	B+F	16.4	10.0	7.0	70.0	—	19.0	10.6	5.3	56.2	—	
132	1.5	123	F	W	B	11.3	10.3	6.8	70.0	—	18.8	11.6	4.9	56.8	—	
125	12	112	M	W	B+C+V	25.2	10.2	6.5	66.3		24.0	9.8	5.6	54.9	—	
1004	1.7	79	F	W	B+F	9.2	10.0	6.7	67.0	—	12.6	10.7	5.8	62.1	—	
226	8	80	M	C	B	20.4	9.5	4.4	41.8		22.6	10.6	4.3	45.6	—	
248	3	88	M	W	B	12.1	10.2	4.3	43.9	—	15.4	11.5	5.5	63.2	—	
218	13	86	M	O	F+C+V	19.7	....	8.0	....	+	23.4	9.7	5.0	48.5	—	
445	9	84	M	O	F+C+V	19.8	9.0	5.4	48.6		22.4	10.2	4.8	49.0	—	
262	7	122	M	C	B+F	15.4	10.0	5.3	53.0	—	18.5	10.3	6.3	64.9	—	
1018	5	82	M	C	B+F	14.2	10.0	5.9	59.0	—	18.5	10.3	5.8	59.7	—	
247	2.5	84	M	W	F+C	9.4	9.0	5.3	47.7	—	13.5	10.4	5.1	53.0	—	
884	1	114	M	C	B	10.2	10.2	6.3	64.3		15.0	11.3	6.1	68.9		
113	5	117	M	O	B+F	11.2	9.9	5.7	56.4	—	15.5	10.7	6.0	64.2	—	
1038	2	101	M	W	B+C+V	18.4	10.7	6.9	73.8		21.4	11.6	5.7	66.1		
131	1.5	121	M	W	B+C	11.1	9.0	7.6	68.4		17.0	10.4	5.0	52.0	—	
1045	7	108	F	C	F+C+V	8.1	7.1	2.5	17.7	+	9.1	9.7	4.7	45.6	..	Scurvy; increased irritability
224	10	99	M	O	F+C+V	22.4	10.0	5.2	52.0	—	24.6	10.9	5.7	62.1	—	
909	14	98	M	O	F+C+V	16.8	9.2	5.6	51.5	—	20.1	10.6	5.2	55.1	—	Malnourished
184	2.5	96	F	C	B	13.2	10.0	5.9	59.6	—	17.0	9.4	6.3	59.2	—	
852	12	111	M	C	F+C+V	19.7	9.0	4.8	43.2	—	21.5	10.7	4.3	46.0	—	
138	4	...	F	W	F	11.7	6.1	7.0	42.7		15.2	10.5	6.3	66.1	—	
Average.....		101	..	..	.....	14.6	9.57	5.94	56.9		17.7	10.6	5.43	57.4		

TABLE 4.—*The Effect on Infants of Plain Diet with no Antirachitic [illegible]*

Average..... 101 .. ..

TABLE 4.—*The Effect on Infants of Plain Diet with no Antirachitic Agent Added*

Number	Age	Duration in Days	Sex	Race	Diet	Initial				Roentgen Observations	Final				Roentgen Observations	Comment
						Weight	Calcium	Phosphorus	Ca × P		Weight	Calcium	Phosphorus	Ca × P		
1002	6	85	F	C	B+C+V	14.7	9.0	3.2	28.8	+	14.6	11.3	4.7	53.1	—	
111	8	122	M	C	B+C+V	16.7	8.1	4.1	33.2	+	16.3	10.3	4.8	49.4	—	Cerebrospinal meningitis 3/1 to 3/18; recovered
208	4	81	F	C	B	12.9	9.6	5.0	48.0	+	14.9	10.8	2.5	27.0	+	
443	10	77	M	C	F+C+V	21.2	9.7	5.7	55.3		22.5	8.8	2.8	24.6	—	
1014	5.5	83	F	W	B	16.4	8.2	4.5	36.9	+	18.4	9.2	5.1	46.9	—	
949	0.8	113	M	C	B	9.7	9.2	5.8	53.4	—	15.3	8.4	3.9	32.8	+	
904	1.5	88	F	C	B	8.3	10.3	4.9	50.5	—	12.1	11.3	4.7	53.1	—	
922	2	80	F	C	B	10.0	9.8	5.7	55.9	—	14.6	10.1	3.9	39.4	—	
919	3	112	F	C	B+F	10.7	10.5	6.5	68.3	—	15.7	10.5	7.0	73.5	—	
1072	7	92	F	C	B+C+V	14.2	9.5	5.2	49.4	—	16.1	8.3	4.3	35.7	—	
878	1.7	106	F	C	B	11.7	11.0	6.9	76.0	—	16.2	10.8	4.0	43.2	±	
877	2	116	F	W	B	11.2	10.5	6.6	69.3	—	16.2	10.5	4.3	45.1	—	2/19/29, purulent conjunctivitis
945	11	106	F	C	B+C+V	18.5	9.7	5.3	51.4	—	19.2	10.5	5.5	57.7	—	
1052	3	82	F	C	B	12.2	8.9	4.9	43.6	+	14.7	6.5	6.1	39.6	+	
228	14	89	F	C	F+C+V	21.1	9.4	5.6	52.6	—	23.8	10.3	5.0	51.5	—	3/27/29, acute suppurative otitis media
976	5	100	F	C	F+C+V	14.1	8.0	2.6	20.8	+	15.3	8.7	2.9	25.2	+	
964	5	112	M	C	B	14.5	8.1	2.9	23.5	+	17.4	9.2	3.2	29.4	—	
881	2.5	111	M	C	B+F	11.5	8.9	6.0	53.4		14.8	6.4	5.4	34.6		
889	3	102	M	C	F	12.2	9.8	6.2	59.8	+	16.1	7.1	4.6	32.7	+	
1074	4	92	F	C	F	12.7	8.6	3.7	31.8		14.4	8.0	2.7	21.6	—	
440	10	89	F	C	F	20.7	7.9	5.0	39.5	—	21.6	8.9	3.7	32.9	+	
194	0.8	107	F	C	B	8.4	....	...	....	—	13.4	9.9	3.8	37.6	—	
252	3	86	M	W	B	14.2	6.7	5.0	33.5	+	17.5	7.5	4.5	33.8	+	
319	2	80	M	C	B+F	12.1	10.0	3.6	36.0	—	16.7	9.9	3.2	31.7	+	
880	5	108	F	W	F+C	13.5	10.5	7.0	73.5	+	16.3	11.0	5.0	55.0	—	
918	10	91	M	C	B+C	18.1	10.3	6.1	62.8	—	19.1	10.2	5.3	54.1	—	
1020	6	113	F	C	B+C	18.2	9.5	6.0	57.0	—	22.0	7.2	4.9	35.3	+	
1047	11	91	M	C	F	20.4	8.0	3.5	28.0		20.2	8.5	2.8	23.8		
1054	8	90	F	C	B+F	16.5	9.8	6.5	63.7	—	19.2	10.0	5.6	56.0	—	
172	11	89	F	W	F+C+V	19.6	10.9	6.1	66.5	—	20.7	11.0	5.6	61.1	—	
1076	3	91	F	C	B+F	13.0	7.1	5.7	40.5	+	17.1	7.7	3.9	30.0	+	
312	11	77	M	C	F+C+V	17.7	9.1	7.6	69.2	—	21.1	9.0	4.2	37.8	—	
327	12	92	F	C	F+C+V	18.4	9.8	5.2	51.0	—	19.7	11.5	5.1	58.6	—	
1043	4	107	M	W	B	17.8	9.5	4.2	39.9	—	21.0	9.7	2.9	28.1	+	
130	2	119	F	W	F	9.6	9.0	8.4	75.6		15.0	8.8	3.4	29.9		
1051	2	97	F	C	B+F	9.4	9.4	6.5	61.1		14.0	7.7	4.9	37.7	—	
162	3	89	M	C	B+F	13.0	10.5	6.1	64.0	—	19.8	10.0	4.4	44.0	—	
998	5	108	F	C	B+F	12.0	7.2	4.5	32.4		13.8	7.4	2.9	21.5		
104	13	136	M	C	F+C+V	12.5	9.2	4.8	44.2	—	15.4	9.5	2.7	25.6	+	Frequent colds
210	5	84	F	C	F	13.1	9.9	5.9	58.4	+	15.2	10.2	4.7	47.9	+	
992	8	89	F	C	F+C+V	13.3	9.6	6.2	59.5	—	15.2	8.8	5.7	50.2	—	
261	2	125	M	C	B	11.8	10.2	7.1	72.4	—	15.4	8.9	4.9	43.6	—	
227	8	84	M	C	F+C+V	18.1	10.5	6.8	71.4	—	19.2	10.9	4.2	45.8	—	
185	2.5	105	M	C	F+V	9.5	8.1	6.2	50.2	+	16.3	....	4.2	....	+	
947	2	111	M	C	B	11.8	8.9	5.9	52.5	—	15.3	9.0	3.3	29.7	—	
178	2	91	F	C	B	10.2	9.5	5.5	52.2	—	13.2	11.0	4.1	45.1	—	
Average		98	..	..	.....	14.2	9.29	5.49	51.5		17.0	9.36	4.29	40.3		

sex, color, weight and diet. There were 18 male, 28 female, 39 colored, 7 white, 26 breast-fed and 20 formula-fed infants (table 5). Their average gain in weight was 2.8 pounds, and the average initial age was 5.5 months. The average blood calcium at the beginning was 9.3 mg. per hundred cubic centimeters; the blood phosphorus was 5.5 mg. per hundred cubic centimeters, and the calcium-phosphorus product was 51.5. At the end of the experiment the average blood calcium was 9.4 mg. per hundred cubic centimeters; the blood phosphorus, 4.3 mg. per hundred cubic centimeters, and the calcium-phosphorus product, 40.3.

TABLE 5.—*Composition of Groups on Basis of Sex, Color and Method of Feeding*

	Male		Female		Colored		White		Breast-Fed		Formula-Fed	
Group	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
Irradiated ergosterol	32	56.1	25	43.9	45	79	12	21	32	56.1	25	43.9
Cod liver oil	36	56.2	28	43.8	44	69	20	31	37	57.8	27	42.2
Cod liver oil plus irradiated ergosterol	32	65.3	17	34.7	33	67.5	16	32.5	23	47	26	53
Control	18	39.2	28	60.8	39	85	7	15	26	56.5	20	43.5

TABLE 6.—*Table of Averages*

			Average Duration of Experiment in Days	Initial				Final			
Group	Initial Age in Mo.	Number of Cases		Wt., Lbs.	Calcium Mg. per 100 Cc.	Phosphorus Mg. per 100 Cc.	Ca×P	Wt., Lbs.	Calcium Mg. per 100 Cc.	Phosphorus Mg. per 100 Cc.	Ca×P
Irradiated ergosterol	5.6	57	98	14.5	9.4	5.3	50.2	17.2	9.5	4.1	39.9
Cod liver oil	6.9	64	101	15.5	9.4	5.5	51.6	18.5	10.7	5.2	56.8
Cod liver oil plus irradiated ergosterol	5.7	49	101	14.6	9.6	5.9	56.9	17.7	10.6	5.4	57.4
Control	5.5	46	98	14.2	9.3	5.5	51.5	17.0	9.4	4.3	40.3

Table 5 gives the composition of the four groups on a basis of sex, color and type of feeding. All the groups are found closely comparable in these respects.

Table 6 gives the number of cases, average initial age, average duration of the experiment, average initial and final weights, average blood calcium and phosphorus in milligrams per hundred cubic centimeters, and average calcium-phosphorus products for the four groups. This is also shown graphically in chart 1. The average ages, gains in weight and average number of days for the groups are closely comparable. The initial average calcium, phosphorus, and calcium-phosphorus products are also similar. The final results, however, give a distinctly different picture, the groups given cod liver oil and cod liver oil plus irradiated ergosterol showing a marked superiority with higher final average determinations on the blood calcium and phosphorus

and higher calcium-phosphorus products. The results for the group given irradiated ergosterol and a control series at the end of the experiment are again much alike. The final average determinations on the blood calcium, and phosphorus and calcium-phosphorus products are all lowered and in about the same degree. This final difference appears to be due chiefly to a decrease in the average phosphorus content of the blood.

Table 7 gives the distribution of cases in the groups according to number and percentage with raised or lowered blood calcium, phosphorus and calcium-phosphorus products. It also shows the initial and final number and percentage of cases in the four groups with a calcium-phos-

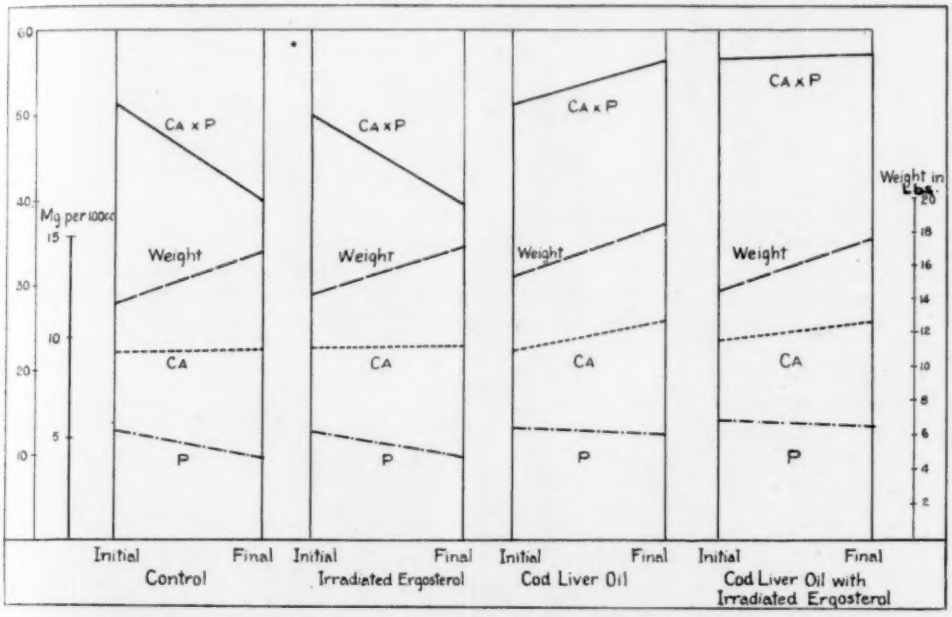

Chart 1.—Average initial and final blood calcium and phosphorus determinations, weights and calcium-phosphorus products for the four groups.

phorus product of 40 or above and those with a calcium-phosphorus product below 40. This is shown graphically in charts 2 and 3. The same division follows here that is seen in table 6—the infants given cod liver oil and cod liver oil plus irradiated ergosterol are definitely superior to those given irradiated ergosterol alone and those used as controls. The final blood calcium was the same or raised in 62 per cent of the controls and in 56 per cent of those given irradiated ergosterol while it was the same or increased in 93 and 85 per cent of those given cod liver oil and cod liver oil plus irradiated ergosterol, respectively. The final blood phosphorus was the same or higher in

18 per cent of the cases in both the group given irradiated ergosterol and the control series but was the same or elevated in 37 and 29 per cent of those given cod liver oil and cod liver oil plus irradiated ergosterol, respectively. The calcium-phosphorus products show still more strikingly these differences; in the group given irradiated ergosterol and in the control group, the calcium-phosphorus products were the

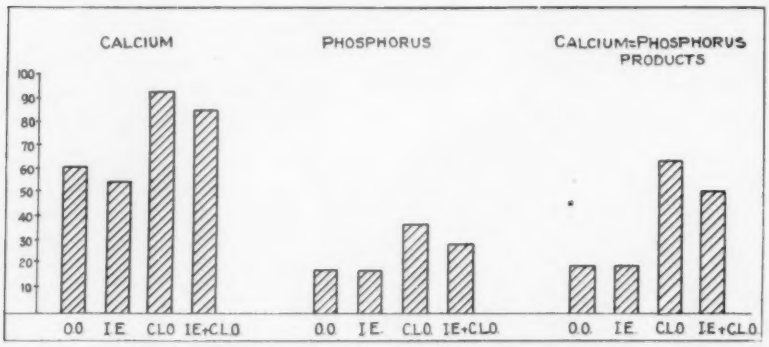

Chart 2.—Final percentile distribution of cases in groups according to raised or lowered blood calcium or phosphorus determinations and calcium-phosphorus products. *O.O.* indicates the central group; *I.E.*, the group given irradiated ergosterol; *C.L.O.*, the group given cod liver oil, and *I.E.+C.L.O.*, the group given cod liver oil plus irradiated ergosterol.

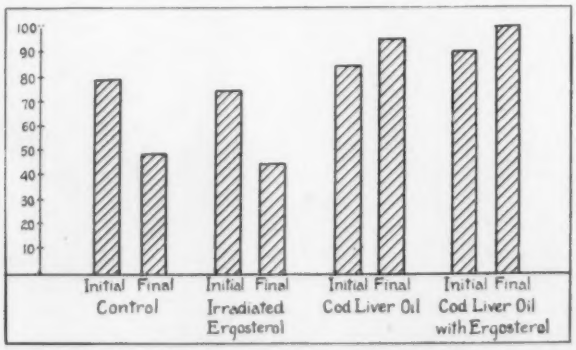

Chart 3.—Percentile distribution of cases according to initial and final calcium-phosphorus products of 40 or above.

same or raised in 21 and 20 per cent, and in those given cod liver oil and cod liver oil plus irradiated ergosterol they were the same or higher in 64 and 51 per cent, respectively. An average initial calcium-phosphorus product of 40 or above was obtained in 75, 84, 90 and 78 per cent, respectively, of those given irradiated ergosterol, cod liver oil, cod liver oil plus irradiated ergosterol and the control series. At the

end of the experiment the same groups gave calcium-phosphorus products of 40 or above in the following percentage of cases: in the group given irradiated ergosterol, 44 per cent; cod liver oil, 95 per cent; cod liver oil plus irradiated ergosterol, 98 per cent, and the control group, 49 per cent. Again the similarity in results for those taking the cod liver oil and the cod liver oil plus irradiated ergosterol as one

TABLE 7.—*Final Distribution of Cases in the Groups According to Raised or Lowered Blood Calcium or Phosphorus Determinations, Calcium-Phosphorus Products and Initial and Final Calcium-Phosphorus Products of 40 or Above*

Group	Total Number of Cases*	Ca Same or Raised	Ca Lower	P Same or Raised	P Lower	Ca × P Raised or Same	Initial		Final	
							Ca×P 40 or Above	Ca×P Below 40	Ca×P 40 or Above	Ca×P Below 40
		No.	No.	No.	No.		No.	No.	No.	No.
Irradiated ergosterol	57	32	25	10	47	12 out of 56	43	14	25	32
Cod liver oil	64	57	4	24	37	39 out of 61	53	10	59	3
Cod liver oil and irradiated ergosterol	49	41	7	14	35	24 out of 47	43	5	48	1
Control	46	28	17	8	37	9 out of 44	35	10	22	23
		Per Cent	Per Cent	Per Cent	Per Cent	Per Cent	Per Cent	Per Cent	Per Cent	Per Cent
Irradiated ergosterol		56	44	18	82	21	75	25	44	56
Cod liver oil		93	7	37	63	64	84	16	95	5
Cod liver oil plus irradiated ergosterol		85	15	29	71	51	90	10	98	2
Control		62	38	18	82	20	78	22	49	51

* When sum of cases does not equal total number of cases, analyses were incomplete.

TABLE 8.—*Percentage of Cases Showing Calcium-Phosphorus Products of 40 or Over, Grouped According to Sex, Color and Type of Feeding*

	Male	Female	White	Colored	Breast-Fed	Formula-Fed
Irradiated ergosterol						
Initial	78.1	72.0	75.0	75.5	83.3	69.2
Final	40.6	48.0	66.7	37.7	26.7	65.4
Cod liver oil						
Initial	74.3	96.4	80.0	86.0	78.9	92.3
Final	97.2	96.2	95.0	95.2	94.4	96.2
Cod liver oil and irradiated ergosterol						
Initial	88.0	94.1	93.8	87.5	91.3	88.0
Final	100.0	94.1	100.0	97.0	95.6	100.0
Control						
Initial	61.16	77.8	57.1	76.32	71.4	76.5
Final	29.4	53.6	57.1	42.1	46.4	43.8

division and for those given irradiated ergosterol and the control group as another is striking.

Table 8 shows the percentage with calcium-phosphorus products of 40 or above according to sex, color and type of feeding, that is, whether breast-fed or formula-fed.

There is no important difference on a basis of sex in the four groups. In the control series and in the group given irradiated ergosterol the percentage of colored infants with calcium-phosphorus products of 40

or above decreased definitely as compared with the white, while the calcium-phosphorus products increased in both the colored and the white infants given cod liver oil and cod liver oil plus irradiated ergosterol. In the group given cod liver oil and cod liver oil plus irradiated ergosterol, there was no significant variation on a basis of color. The breast-fed infants in the group given irradiated ergosterol stood out as showing the greatest percentage of decrease in the calcium-phosphorus product. In the control group, both the breast-fed and the formula-fed infants showed a marked decrease. No other important difference was noted according to type of feeding.

CONCLUSIONS

1. Cod liver oil prevented or cured rickets in 95 per cent of the cases studied when given in a dosage of 3 teaspoonfuls daily (1,400 rat units of vitamin D). Considering the subjects who were normal or improved at the end of the experiment, 98 per cent were either well or benefited.

2. A mixture of cod liver oil plus irradiated ergosterol in a dosage of 3 teaspoonfuls (3,750 rat units of vitamin D daily) prevented or cured rickets in 98 per cent of the cases.

There was no evidence of superiority among this group as compared with the group given cod liver oil.

3. Irradiated ergosterol in a daily dosage of 1,250 rat units of vitamin D prevented or cured rickets in only 44 per cent of the cases studied. The results in this group were not significantly better than those for the control group of untreated subjects.

4. Cod liver oil in a dosage of 1,400 rat units of vitamin D per day was a much more satisfactory antirachitic agent than was the irradiated ergosterol in the approximately equivalent rat unit dosage. It would seem that we are not justified in considering rat units of vitamin D in irradiated ergosterol as being equivalent to the same number of rat units of vitamin D in cod liver oil as a curative or prophylactic remedy for rickets.

5. There is no definite evidence of a greater incidence of rickets among formula-fed than among breast-fed infants.

6. There is evidence of a greater need for protection against rickets among the colored infants, as is shown by the greater final incidence of rickets among these infants in the control series and in the group given irradiated ergosterol. It is also clear that these infants are protected successfully by a daily dose of 3 teaspoonfuls of cod liver oil (1,400 rat units).

LYMPHATIC LEUKEMIA WITHOUT LEUKOCYTOSIS *

C. M. HYLAND, M.D.
LOS ANGELES

In reviewing the literature on leukemia in which the disease is not accompanied by leukocytosis, one is immediately aware that such a condition has been recognized only in recent years, and also that reports of such cases are infrequent enough for one to look on them as of rather rare occurrence. Such a condition has been variously referred to as aleukemic leukemia, pseudoleukemia, leukemia with leukopenia and leukemia without leukocytosis.

Many writers refer to aleukemic phases in true leukemias, and a terminal leukemia is often observed in cases that throughout their course were considered typical; but cases showing no abnormal increase in the total white count throughout the entire illness are hard to find, especially if these cases are observed for any length of time. Litchfield [1] reported the cases of two patients, one, aged 9 years, who had 7,000 white cells with 95 per cent lymphocytes. The second patient, aged 6 months, on one occasion had a total white count of 5,200 with 94 per cent lymphocytes and on another occasion 3,700 white cells with 93 per cent lymphocytes. The former patient was under observation approximately six weeks and the latter for approximately three weeks.

Bass [2] reported the case of a child, aged 4 years, in whom the white cells varied from 1,800 to 4,000 and the lymphocytes from 64 to 86 per cent. The prominent symptoms in this case were high fever, abdominal pain, pain in the ankles and legs and a purpuric eruption. This case was classified as lymphatic leukemia, the basis being the relative and absolute lymphocytosis, although there was no statement as to how long the case was under observation.

Washburn [3] reported two cases of this condition although one of the patients, V. L., showed 22,000 white cells at one time, and the other, J. M., showed 16,000 on one occasion. Blankenhorn and Goldblatt [4] stated that in a series of fifty-two cases of leukemia in Lakeside Hos-

* Submitted for publication, Aug. 21, 1929.

* From the Pathological Laboratories of Children's Hospital.

1. Litchfield, W. F.: A Series of Cases of Primary Anaemia in Children, M. J. Australia **1**:231 (March 19) 1921.

2. Bass, Murray H.: Leukemia in Children, Am. J. M. Sc. **162**:647 (Nov.) 1921.

3. Washburn, Alfred H.: Lymphatic Leukemia with Leukopenia in Young Children, Am. J. Dis. Child. **29**:631 (May) 1925.

4. Blankenhorn, M. A., and Goldblatt, H.: Aleukemic Leukemia with Unusual Skin Manifestations, J. A. M. A. **76**:585 (Feb. 26) 1921.

pital three were never seen with an abnormal leukocyte count, although the length of time these cases were under observation is not given. Crawford [5] reported the case of an adult who showed 8,900 white cells with 77 per cent mononuclears; however, the patient was only under observation for twelve days and this might represent the terminal aleukemic phase referred to.

At the Children's Hospital during the past year, three cases have been observed which have been classified as leukemia, and during the entire period of their observation the highest white count recorded in any case was 8,600.

REPORT OF CASES

CASE 1.—*History.*—J. L., a boy, aged 5½ years, was admitted to the hospital on Feb. 18, 1929, in the service of Dr. Fish, the chief complaint being fever, constipation and jaundice. Just before Christmas he had what was called influenza and since had been fatigued and felt bad most of the time. One week before admission he was jaundiced and had clay-colored stools. He was constipated most of the time. At the onset of the jaundice he had a rise in temperature that reached 105 F.

The patient was born after a full-term normal delivery. The labor lasted for three hours. The birth weight was 7½ pounds (3.4 Kg.). He was breast-fed for nine months. He walked at 1 year. One year before admission he had convulsions, with a temperature of 104 F. that was never explained.

Examination.—On admission, the boy was pale, moderately prostrated, of good nutrition, and had an injected pharynx. The tonsils were submerged, and the mucous membranes were very pale. There was a marked cervical adenopathy. A systolic murmur was present over the precordium, and the liver was two fingerbreadths below the costal margin. He did not appear jaundiced and the fever was gradually on the decline.

Laboratory Observations.—Examination on admission showed: erythrocytes, 1,370,000 per cubic millimeter; hemoglobin, 20 per cent (Daré); leukocytes, 640. The differential count showed lymphocytes, 68 per cent; polymorphonuclears, 22 per cent; basophils, 2 per cent, and transitionals, 8 per cent. The reticulated red cells numbered 1 in 500 cells. The clot retraction was normal. The urinalysis gave negative results on many examinations.

X-ray films were interpreted as showing a dense right antrum and thickening of the walls of the left antrum.

The fragility test began at 0.5 and ended at 0.32. The Wassermann and Kahn tests gave negative results. The blood culture was negative. Subsequent work on the blood is recorded in table 1. (Normoblasts are not listed in this table but were present in virtually all of the counts.)

Course of Illness.—On February 22, the patient was given 205 cc. of citrated blood intravenously. He was discharged on February 25, returning to his home; on March 7, he began to have a fever, the temperature ranging between 102 to 104 F. On March 9, he was admitted to another hospital for a transfusion and received 225 cc. of citrated blood. He returned home the same day.

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5. Crawford, Baxter L., and Weiss, Edward: Chronic Lymphatic Leukemia with Aleukemic Blood Picture, J. A. M. A. **90**:203 (Jan. 21) 1928.

On March 13, he was admitted to the Children's Hospital a great deal weaker, showing marked enlargement of the anterior cervical glands on both sides, also enlargement of the axillary, epitrochlear and inguinal glands. The spleen was palpable, the liver reached nearly to the umbilicus and the skin was a marked lemon yellow color.

On March 16, a transfusion of 130 cc. of citrated blood was given intravenously; on March 18, the right antrum was punctured, no pus being obtained, and it was necessary to pack the antrum to control the hemorrhage. Culture of the material obtained from this puncture showed *Streptococcus viridans.*

During the entire course of the illness, the patient grew progressively worse, and he died on March 19.

Necropsy (March 19).—The body was that of a white boy, aged 5½ years, measuring 117 cm. in length and showing enlargement of the cervical, axillary, epitrochlear and inguinal glands. The heart showed several small irregular hemorrhages beneath the epicardium. Both lungs showed irregular subpleural hemorrhages over their entire surface and marked hyperplasia of the lymph glands about the hilum. The liver was large, weighing 880 Gm., and many irregular lighter areas were observed on the external surface as well as on the cut surface. The spleen weighed 145 Gm., and measured 12 by 7 by 3 cm. The pulp was

TABLE 1.—*Observations on the Blood in Case 1*

Date	Hemoglobin, Per Cent	Red Blood Cells	White Blood Cells	Lymphocytes	Polymorphonuclears	Basophils	Transitionals	Platelets	Bleeding Time	Clotting Time
2/20/29			2,775	22	68		10			
2/21/29		1,780,060	1,950					220,000		
2/22/29								160,000		
2/26/29	25	1,780,000	1,850	70	20		10			
3/ 4/29	28	1,860,000	2,600	38	57	1	4			
3/14/29	34	1,740,000	1,450	90	10				3 min.	3 min.

somewhat soft, and the trabecula and follicles were invisible. Microscopic sections showed masses of lymphocytes beneath the capsule of the liver and masses of lymphoid cells throughout the entire liver substance not occupying any special location with regard to the lobules of the liver. In the kidney sections masses of lymphocytes were found throughout. In the spleen there was much infiltration by lymphoid cells in the subendothelium of the sinuses. The lymph glands showed a complete loss of architecture accounted for by the diffuse masses of lymphocytes present in all sections of the gland examined. The sections of the bone marrow showed some hyperplasia of the erythroblastic centers and islands of lymphoid infiltration.

CASE 2.—J. J. S., a boy, aged 5 years, was admitted to Lane Hospital, San Francisco, on March 8, 1928, with the chief complaint of anemia since appendectomy, following an attack of abdominal pain associated with fever on Dec. 29, 1927. Since that time he had had intermittent attacks of pain in the right arm and knees. The essential physical observations were moderate pallor and moderately hypertrophied tonsils.

Laboratory Observations.—The urine was normal; the Wassermann reaction was negative. Blood counts taken during this hospital admission are shown in table 2.

The fragility test showed hemolysis beginning at 0.26 and complete at 0.18 per cent. The patient was given liver extract for two weeks during his stay in

the hospital. A transfusion was given on March 30, 1928. The patient returned to the hospital on April 23 for another transfusion and for three weeks appeared much improved.

On June 14, he was admitted to Children's Hospital, Los Angeles, on the service of Dr. Stork, complaining of attacks of acute abdominal pain and fever recurring every three or four days in the interval between April 23, 1928, and the date of admission to this hospital.

History.—Delivery was by instrument. The birth weight was 4 pounds (1.8 Kg.). The infant was two weeks premature. He did not have any of the diseases of childhood. The parents were living and well. Examination on admission showed a child of good nutrition with a pale yellowish skin. The liver was two fingerbreadths below the costal margin. The spleen was not palpable, and a soft systolic murmur was present over the apex.

Subsequent Laboratory Observations.—The urine was normal. The tuberculin test, with 0.1 mg. of tuberculin, was negative in forty-eight hours. The kidney function was 55 per cent in two hours. Blood cultures taken on July 21, 1928,

TABLE 2.—*Observations on the Blood in Case 2, During the First Admission*

Date	Hemoglobin, Per Cent	Red Blood Cells	White Blood Cells	Differential Count, Per Cent	Reticular Cells		
					Normoblasts*	Per Cent	Platelets
3/8 /28	45	2,500,000	5,200	63 lymphocytes	1	0.5	190,000
3/10/28	47	2,700,000	5,550				
3/15/28	50	3,000,000	5,150	63 lymphocytes		1.5	
3/19/28	45	2,400,000	6,000			1.0	
3/22/28	47	2,230,000	4,640	73 lymphocytes	1	1.8	
3/24/28		2,300,000	5,250	59 lymphocytes		1.7	
3/26/28	43	2,120,000				1.6	
3/28/28	40	2,020,000	3,250	85 lymphocytes		1.5	
3/30/28	35	1,920,000	3,560	85 lymphocytes	3	1.4	
4/2 /28	55	2,960,000	2,600	55 lymphocytes	4	0.7	
4/9/ 28	70	3,640,000	5,550	64 lymphocytes	1	1.8	
4/23/28	53	2,410,000	4,800	73 lymphocytes	1	0.8	
4/26/28	66	3,350,000	3,950	71 polymorphonuclears			160,000
5/2 /28	80	4,280,000	5,250	76 lymphocytes		0.2	

* Normoblasts indicate cells per hundred white blood cells.

and on March 21, 1929, were negative. Observations on the blood during the course of the disease are listed in table 3.

Course.—While in the hospital, the patient complained of severe pain in the lower part of the back and in the right thigh and was given transfusions on the dates indicated in table 3. He was discharged on July 22, 1928. There were many subsequent admissions for transfusions, as indicated in table 3. After all transfusions a temporary benefit would be noticed, and his condition would seem about the same on each entry except that the pains were becoming more severe and he was getting progressively weaker. In the interval between admissions there was always fever for a few days at a time. On Oct. 2, 1928, for the first time in the illness it was noted that the lymph nodes in the axilla and groin were enlarged, and on Jan. 4, 1929, the anterior cervical glands were found to be enlarged. During January, the patient was confined to his bed at all times and was losing strength rapidly; death occurred on March 31, in the White Memorial Hospital, Los Angeles.

Necropsy.—(The data were furnished by Dr. Pratt, Pathologist, White Memorial Hospital.) A well nourished child, aged 5 years, showing enlargement of the anterior, cervical, axillary and inguinal lymph nodes was seen. He was very anemic in appearance and showed several purpuric spots scattered over the body

and also a few areas of hemorrhage beneath the visceral pleura of both lungs. Much free blood was present in the stomach and intestines, also massive subcapsular hemorrhages of both kidneys, shown on cut section to be practically confined to the cortex. The liver was greatly enlarged, weighing 1,350 Gm., and was brownish. On section, the surface was seen to be mottled with numerous small yellow areas. Microscopic sections of the liver showed small areas of lymphoid infiltration replacing the liver tissue and compressing the liver cords. The kid-

TABLE 3.—*Observation on the Blood in Case 2, During Course of Disease* *

Date	Hemoglobin	Red Blood Cells	White Blood Cells	Lymphocytes	Polymorphonuclears	Others	Platelets	Bleeding Time	Clotting Time
6/14/28	55	3,280,000	6,684	69	31		300,000	3 min.	2 min.
6/22/28	50	2,020,000	5,600	78	22		130,000		
6/29/28	20	1,460,000	3,450						
7/6 /28		Transfusion							
7/10/28	38	1,950,000							
7/18/28	38	1,930,000	2,450	82	18	0.5% Reticulated red			
7/20/28	45	2,540,000	3,600	78	22				
7/21/28			3,700				100,000		
8/8 /28	36	1,860,000	3,040	91	7				
8/8 /28		Transfusion							
8/10/28	45	2,530,000	1,150	75	25				
9/22/28	18	1,440,000	3,978	74	26				
9/24/28		Transfusion							
9/25/28	30	2,380,000	2,000					3½ min.	7 min.
9/28/28	30	2,480,000	4,500	92	8	0.2% Reticulated red	120,000		
10/5 /28		Transfusion							
10/7 /28	32	2,300,000	4,200	90	10				
11/1 /28	20	1,130,000	6,366	88	12				
11/17/28		Transfusion							
12/5 /28	23	1,320,000	2,705	83	15	2% Reticulated red			
12/6 /28		Transfusion							
1/7 /29	30	1,670,000	3,976	79	20	1% Reticulated red			
1/8 /29	30	1,670,000							
1/9 /29		Transfusion							
1/26/29	24	1,300,000	3,183	88	12				
2/13/29	10	940,000	4,615	66	34	Baso myelocyte 1			
2/14/29		Transfusion							
2/15/29	20	2,080,000							
2/16/29		Transfusion							
2/17/29	30	2,630,000							
3/16/29	10	780,000	4,700	76	24		50,000		
3/19/29		Transfusion							
3/21/29	18	1,350,000	3,500						
3/22/29				86	14	0.5% Reticulated red		6 min.	3 min.
3/25/29		Transfusion							
3/26/29	28	2,400,000	4,000						
3/31/29		Patient died							

* Normoblasts are not listed in the table but were present in many of the counts.

neys showed degeneration of the tubular epithelium and lymphoid infiltration of the kidney substance together with many areas of hemorrhage.

CASE 3.—*History.*—R. S., a boy, aged 8½ years, was admitted to the hospital on Nov. 4, 1928, in the service of Dr. Fish, the chief complaint being generalized weakness dating back for five months. He was in good health until June, 1928, and following administration of toxin-antitoxin mixture, his mother noticed that the child looked pale, his appetite failed and he did not gain in weight. During the latter part of August, he had a sudden onset of fever, reaching 102 F., which was accompanied by vomiting. He also had frequent bleeding from the gums. The weakness progressed, with periods of remission, and about November 1 he had abdominal cramps, also pain in the legs and left side of the chest.

The patient was born at full-term and was breast fed for thirteen months. At the age of 1 year he weighed 32 pounds (14.5 Kg.), and at 2 years, 38 pounds (17.2 Kg.). He had whooping cough and measles in infancy. There had been no contacts with tuberculous patients.

Examination.—Examination showed a poorly nourished, very pale boy with several carious teeth, also enlargement of the posterior cervical, axillary and inguinal glands. The heart was slightly enlarged to the left with a systolic murmur over the apex which was transmitted to the angle of the scapula.

Laboratory Observations.—On many occasions urinalysis showed 2 plus albumin and from 15 to 20 pus cells per high power field. One-tenth milligram of tuberculin was negative in twenty-four hours. The Wassermann reaction was negative. Examinations on the blood and the dates of the transfusions are recorded in table 4.

Course of Illness.—During the entire illness, the course of which was marked by three hospital admissions and a like number of discharges, the patient's course continued progressively downward, the bleeding from the gums continued, the glandular enlargement was progressive and the abdominal cramps, pain in the

TABLE 4.—*Examinations of Blood and Dates of Transfusions in Case 3* *

Date	Hemoglobin	Red Blood Cells	White Blood Cells	Lymphocytes	Polymorphonuclears	Transitionals	Platelets	Clotting Time	Bleeding Time
11/2 /28	28	1,830,000	8,600	96	4		120,000	7 min.	2½ min.
11/5 /28	30	1,510,000	5,880	79	19	2			
11/16/28		Transfusion							
11/24/28		Transfusion							
12/4 /28		Transfusion							
1/3 /29	10	620,000	6,684	92	8				
1/3 /29		Transfusion							
1/10/29		Transfusion							
1/29/29		Transfusion							
2/20/29	15	1,190,000	5,729	89	10	1			
2/21/29		Transfusion							

* Normoblasts are not listed in the table but were present in many of the counts.

legs and vomiting continued. The last discharge was on Feb. 22, 1929, and death occurred at his home a few days later. No autopsy was obtained.

COMMENT

Three cases are reported of lymphatic leukemia without leukocytosis, two of the cases coming to autopsy and presenting the pathologic observations of leukemia. The patient in case 3 died at home, and his death was not learned of in time for any effort to be made to secure an autopsy. His illness was so typical of the other cases that throughout the course of the illness he was considered to have leukemia of the type in question.

All of the cases were characterized by glandular enlargement, although in case 2 this did not manifest itself until seven months after the beginning of the illness, while in the other cases this condition was observed on the first examination.

All cases throughout their course showed a severe anemia in which transfusions were only of temporary value.

All cases were characterized by fever, and two of the patients had severe pain throughout the illness.

In one case, hemorrhage from the gums was a prominent feature and in another bleeding was rather severe after antrum puncture.

In one case, the parent associated the inception of the condition with a previous appendectomy, and in another instance to the administration of toxin-antitoxin.

A striking feature in all of the cases was the low white cell count, 8,600 being the highest number recorded in any case. The high percentage of lymphocytes in all cases was also striking. It will be noticed that immature or unclassified forms are not listed in the various counts, excepting that on one occasion a myelocyte was found in case 2. Slides from all the cases were studied by many persons, and at no time were cells encountered that offered difficulty in their classification.

4614 Sunset Boulevard.

SCARLET FEVER TOXOID*

H. O. McMAHON, M.D.
MILWAUKEE

Since Gabritschewsky, in 1907, proposed the use of a vaccine made of the culture fluid of streptococci to secure an immunization against scarlet fever, much effort has been expended and various types of immunizing agents have been produced, each numbering among its adherents many investigators ready to produce figures and case reports of considerable proportions; this induced an enthusiasm which has undoubtedly given the incentive to immunize large numbers of persons against this disease. Before proceeding with my report concerning immunization by toxoid, the material for which was furnished by Dr. Donald Fraser of the Connaught Laboratories, University of Toronto, it may be well to digress with a cursory review of the literature and some figures as to the relative values of the various methods of immunization in use at this time.

When Gabritschewsky, with his first dose of 0.5 cc. of vaccine, produced a rash similar to that of scarlet fever in 13 per cent of the children, it probably contained between 2,500 and 5,000 Dick skin test doses. As the second dose was double the quantity of the first and the third was double the quantity of the second, he probably gave, in the three injections, about 25,000 skin test doses. This work was carried on by others after his death. They reported that the vaccinated children in that village of Russia in which scarlet fever is so abundant rarely develop the disease, while the unvaccinated children frequently do.

The brilliant discovery of the Dicks that the filtrate of the culture could be used when given in proper dilution as a test for immunity in the same way as the Schick test is used for diphtheria made possible the selection of those who needed immunization, gave a method of determining the duration of immunity and allowed also the estimation of the amount of toxin given in the immunizing injection. It was found that moderate amounts given in from three to five doses at intervals of one week or more produced immunity in a short time in a majority of children. However, severe reactions have been reported following its use.

Park, in his early attempts to immunize children against scarlet fever, gave small doses of toxin; 1,500 skin test doses, divided into three injections. The results were fairly good, but the immunity did not last. The dosage was then increased to 12,000 skin test doses, divided into

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* Department of Pediatrics, Marquette University Medical School.

five injections; 700, 1,200, 3,000 and 4,000 and 5,000 skin test doses. This gave, at the end of four weeks, 91 per cent immune subjects, but the immunity with the dosage did not last beyond six months in many of the children who had given a more positive reaction. The dosage has been further increased until now he is using 1,000, 5,000, 10,000, 15,000 and 30,000 skin test doses given at weekly intervals.

In the *Journal of the American Medical Association,* the Dicks [1] gave a table showing the increased amount of immunizing power of different dosages; when 1,000 to 2,000 skin test doses are given, they find that 14 per cent of the children become completely immunized; when 5,000 to 6,000 skin test doses are given, 66 per cent of the children are immune and from 10,000 to 12,500 doses, 91 per cent. The experience of practically all observers has been that the small doses are not lasting, and the dosage and number of injections have been mounting until these large figures have been reached. Such large doses are given with the hope of producing a lasting immunity. A few years will tell whether it will be necessary to give another series of large doses to obtain prolonged immunity.

Dr. G. L. Keifer, commissioner of the department of health, Michigan, reported that the present practice in that state is to give three doses, two weeks apart, of 500, 3,500 and 30,000 skin test doses. This course is yielding a high immunization rate. On the other hand, it is of interest that Kinloch, Smith and Taylor, with much smaller doses, weekly injections of 500, 1,000 and 3,000 skin test doses, record a negative Dick reaction percentage of 75 in four months.

Zelikina and Kuritzina were able to lower materially the toxicity of scarlet fever toxin prepared according to the method of Dick, without losing its antigenic property, by the addition of 1 per cent formaldehyde solution, and by keeping it in a thermostat at 40 to 42 C. for five weeks. Administration of large doses of anatoxin on two occasions, 4,500 skin test doses the first time and 30,000 the second time, resulted in conversion of a positive Dick reaction to a negative reaction in a high percentage of cases without producing a marked reaction on the part of the organism. In 100 children immunized by this method, 80 exhibited a change from positive to a negative reaction; in 13 it became weaker, and in 7 it was not influenced.

Benson of Edinburgh, in 1928, in reporting the immunization of nurses, said that in the use of toxoid one third of the group of 78 complained of constitutional reaction after either the first or the second dose, but none after the final dose. Constitutional symptoms occurred

1. Dick, G. F., and Dick, G. H.: Therapeutic Results with Concentrated Scarlet Fever Antitoxin, Preliminary Report; Preparation, Standardization, and Dosage of Antitoxin, J. A. M. A. **84**:1477 (May 16) 1925.

in persons showing a large scarlet red reaction to the Dick test. He suggested for these persons the use of smaller dosage.

Dr. Fraser reported on the results of testing 45 girls, three weeks after the last dose of his toxoid, 57 per cent negative reactions to two skin test doses, 36 per cent negative to five skin test doses and 43 per cent positive reactions to two skin test doses. He claimed no undesirable reactions in this series of cases.

On April 4 and 5, 1929, 176 institutional children ranging in age from 4 years to 16 years were given the Dick test. Of this number, 55, a trifle less than 30 per cent, gave positive reactions. In the interpretation of the Dick test, I took all reactions over 5 mm. to be positive. These 55 patients were given the first inoculation, consisting of 0.5 cc. of scarlet fever toxoid, on April 15. On May 6, they were given the second inoculation of 1 cc. and on May 31 the third and final dose of 1.5 cc. On August 15, these children received another Dick test, and to be certain they had not been sensitized by the three injections of toxoid, I incorporated a test with diluted toxoid; 1 to 1,500 of the same concentration approximately, as was used in the toxin to make up the Dick test. The final reading showed 3 persons with positive reactions less than 5 mm. and 4 with positive reactions as high as 10 mm. One gave a pronounced positive reaction from both the Dick test and diluted toxoid. I believe I am safe in affirming that in this series of cases the reaction of 5 mm. and under, may safely be considered negative; consequently, I have 4 positive reactions in 55 cases, or approximately 72 per cent of immunization.

I had but one reaction of any consequence. A 14 year old girl developed a high temperature and was kept in bed for two days following her second inoculation. She had no trouble at her next inoculation. Two of the smaller children developed a slight rise in temperature, but were able to be about their regular duties the following day.

It is a debatable question as to how, generally, scarlet fever vaccine should be employed. Scarlet fever is a rather mild disease in most sections of the country, but the complications may be severe. The deaths in New York City, for instance, are less than 1 in 100,000 persons. The number of cases annually, however, ranges from 10,000 to 20,000. While immunization is rapid, it is not always lasting, so that one cannot expect to develop an immune population.

Park urged that all nurses who expect to be in contact with scarlet fever patients should be immunized, as should all children in institutions. He advised immunization in schools and families in which exposure to scarlet fever is imminent because of outbreaks in the neighborhood. But when a case of scarlet fever breaks out in a family or institution, he prefers to perform a Dick test on the inmates and to begin active immunization of those who have been exposed rather than to give scarlet

fever antitoxin. The scarlet fever antitoxin gives an immunization lasting only from ten days to two weeks, and at present is more apt to produce serum sickness when injected into human beings than does diphtheria antitoxin.

Toxoid has, in my opinion, certain advantages. In the first place, three injections are required as against five for toxin.

There is no danger of sensitization to horse serum.

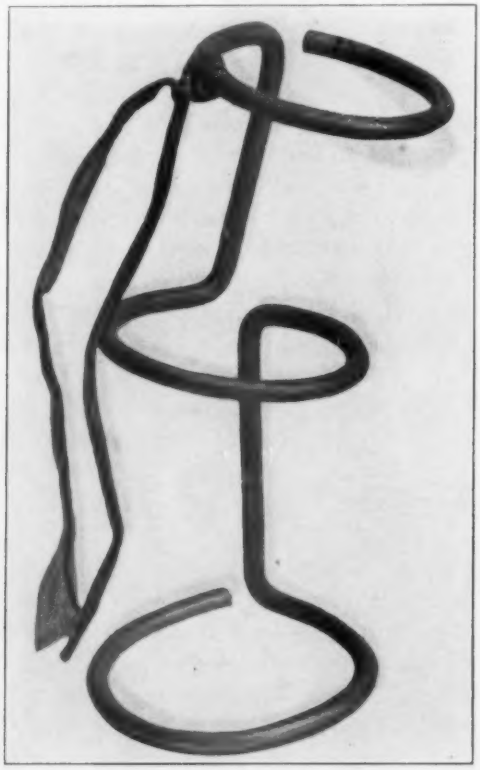
The reactions are of no great consequence.

The percentage of negative Dick skin reactions compares favorably with other methods. The increase of diphtheria toxoid gives an indication of the favorable results obtained from this method of immunization.

THUMB SUCKING APPARATUS*

W. W. ANDERSON, M.D.
ATLANTA, GA.

This apparatus is made of aluminum wire, three sixteenths of an inch in diameter, according to measurements of the infant's arms. The apparatus shown in the accompanying figure measures 5½ inches in its longest measurements. The three rings are 1¾, 1⅞ and 2½ inches,



Thumb sucking apparatus.

respectively, in diameter. It is bent at a slight degree to conform to the infant's arm. It has the advantages over the common paper cuff in that it is light, cool, more durable and easily sterilized. It is inexpensive and can be easily made in a short while. I am submitting it on account of its simplicity, comfort and efficiency.

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NEW METHOD FOR THE DETERMINATION OF THE BASAL METABOLISM OF BABIES AND OF SMALL CHILDREN*

HAROLD L. HIGGINS, M.D.
AND
VELMA BATES
BOSTON

A suitable and satisfactory determination of the basal metabolism requires (1) an accurate measurement of the carbon dioxide elimination or of the oxygen consumption and (2) a resting, quiet subject. In young children and in infants both of these factors present different problems than in adults. The mouthpiece, or mask, is not feasible for infants, and a chamber, or box, is usually used. Infants produce much less carbon dioxide than adults, and for accurate gravimetric determinations of the carbon dioxide production rather long periods of at least from thirty to sixty minutes have been required. The average baby or small child usually is restless or may cry, especially if under observation for some time; this is undoubtedly the main difficulty and source of error in determining their basal metabolism.

During the past year at the children's clinic of the Massachusetts General Hospital, a new method of determining the basal metabolism of babies and small children has been employed. Many of the fundamental features of the method previously used—that of Benedict and Talbot [1]—are retained, but instead of the observation requiring two or three hours, it now takes from two to four minutes for a single test and from twenty-five to forty-five minutes for the whole study of the child. The child's activity is less and the determination much more satisfactory. The actual technical accuracy of the measurement of carbon dioxide elimination and oxygen consumption has also been increased.

APPARATUS

The apparatus for the determinations consists of: (1) A chamber in which the child is placed. Those described by Benedict and Talbot [2] have been used. The smaller box has a capacity of 84 liters, which

* Submitted for publication, Oct. 5, 1929.

* From the Children's Medical Service, Massachusetts General Hospital.

1. Benedict, F. G., and Talbot, F. B.: The Gaseous Metabolism of Infants, Washington, D. C., Carnegie Institution of Washington, 1914, pub. 201.

2. Benedict, F. G., and Talbot, F. B.: Metabolism and Growth from Birth to Puberty, Washington, D. C., Carnegie Institution of Washington, 1921, pub. 302, p. 28; Study in the Respiratory Exchange of Infants, Am. J. Dis. Child. **8**:1 (July) 1914.

when corrected for the volume of the mattress and the baby is reduced to 75 liters. The larger box has an uncorrected volume of 472 liters. (2) A blower with rheostat connection to the operating motor so that a ventilation of from 8 to 30 liters per minute may be obtained. The blower made by Gilman Crowell Company of Brooklyn has been used. (3) A calibrated gasometer with a capacity of 100 liters, with a graduated scale. (4) Gas samplers with a capacity of approximately 150 cc. (5) A gas analysis apparatus of Haldane-Carpenter.[3] This analyzes a sample of 40 cc. of air for carbon dioxide and oxygen with an accuracy of 0.003 per cent of the total volume; as the percentage carbon dioxide

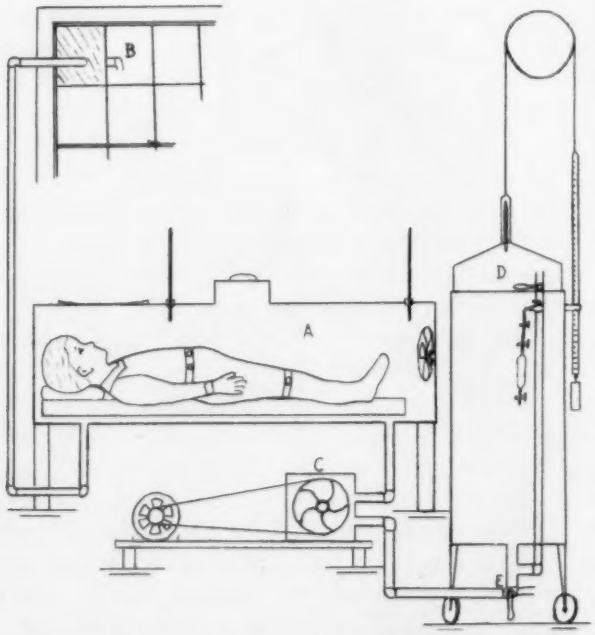

Fig. 1.—Apparatus for determination of basal metabolism in infants. *A* indicates the box; *B*, the outdoors; *C*, the blower; *D*, the gasometer; *E*, the gasometer valve.

or oxygen deficit is usually about 0.400 in our observations, the accuracy is better than 1 per cent in the measurement of these gases.

The scheme of the apparatus is shown in figure 1. Air is drawn through the box, *A*, from outdoors, *B*, and sent by the blower, *C*, into the gasometer, *D*. Until the period of observation begins, the air passes

3. Carpenter, T. M.: An Apparatus for the Exact Analysis of Air in Metabolism Investigations with Respiratory Exchange Chambers, J. M. Research **4**:1 (July) 1923. Carpenter, T. M.; Fox, E. L., and Sereque, A. F.: The Carpenter Form of the Haldane Gas Analysis Apparatus: Changes Made in the Apparatus and Details Regarding Its Use, J. Biol. Chem. **83**:211 (July) 1929.

through the gasometer valve, *E*, into the room. It is customary not to start the collection of air from the box until the child has been lying quietly for from ten to twenty minutes. The period is begun by turning the valve, *E*, to let air into the gasometer. The air is collected for a measured period of time (between two and four minutes); then the valve is again shut off. The volume and temperature of the air in the bell are read, and a sample is collected; in collecting the sample, it is our custom to use suction from an ordinary water pump to draw the air through the gas sampler. The gasometer is emptied and another period started as soon as possible. Four such periods are sufficient to get

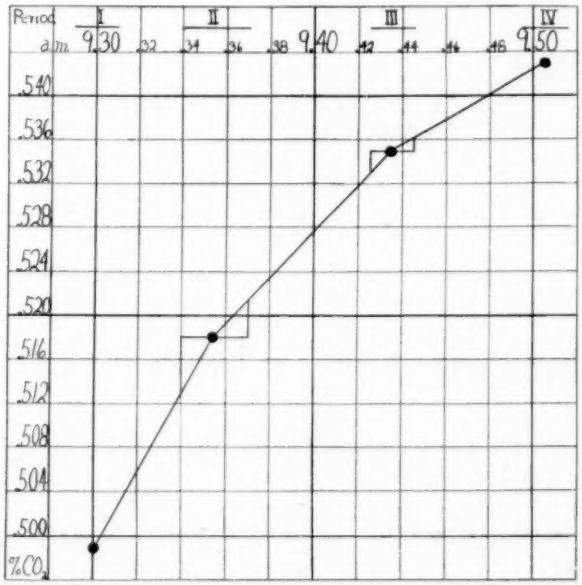

Fig. 2.—Curve of the carbon dioxide in the box; the dots mark the middle of each period and the carbon dioxide content of the air collected in that period.

satisfactory results. The air collected is analyzed for percentage carbon dioxide. One sample is also analyzed for percentage oxygen; from this the respiratory quotient is calculated; an accurate knowledge of the caloric value of the carbon dioxide production of the patient is thus possible.

Correction must be made for change in residual amount of carbon dioxide in the box, between the start and finish of each period. To do this a curve of the carbon dioxide in the box is plotted, the dots marking the middle of each period and the carbon dioxide content of the air collected in that period (fig. 2). On this chart the beginning and end of the period are plotted, and the difference is taken to show the residual change.

DETERMINATION OF METABOLISM

Data and calculations of the determination of the metabolism of one of our patients are given:

Patient: Ruth L.
Age: 7 years and 8 months.
Diagnosis: thyroid deficiency (?)
Date: March 6, 1929.
Barometer: 739.3 mm.
Temperature, room: 22.6 C.
Temperature, box: 24 C.
In large box at 9:07 a. m.
Motor started at 9:12 a. m.

Weight with clothes: 16.13 Kg.
Weight without clothes: 15.51 Kg.
Height: 96.5 cm.
Body surface: 0.646 sq.m.
Awake and cooperative.
No breakfast.
Temperature: 99.8 F. (mouth).
Pulse rate: 92.

Period			I	II	III	IV
Activity	none	none	none	none	none	slight
Time:						
Start	9.14	9.24	9.29	9.34	9.42½	9.49½
End	9.15	9.25	9.31	9.37	9.44½	9.51½
Gasometer Reading:						
Start	0.30	0.30	0.31	0.33	0.54	0.55
End	11.73	12.50	24.98	38.68	26.61	26.96
Temperature			21.4	21.7	21.7	21.9
Percentage carbon dioxide			0.499	0.518	0.535	0.543
Percentage oxygen					20.355	
Results:						
Respiratory quotient					0.83	
Total metabolism				716	701	

Calculation of Period III

1.343 liters = 1.00 on gasometer scale
× 26.07 change in gasometer reading

35.2 liters of air leaving chamber (*A*)
472 liters; gross volume of box
— 23 volume of child, spring, mattress and pillow

449 liters, corrected volume of box (*B*)
0.533 per cent carbon dioxide in box at start of period (obtained from fig. 2)
0.536 per cent in box at end of period

0.003 per cent difference (*C*)
449 liters (*B*)
× 0.003 per cent (*C*)

0.013 liters of carbon dioxide more in box at end of period than at start (*D*)
0.535 per cent carbon dioxide in air leaving chamber
— 0.030 per cent carbon dioxide in air entering chamber

0.505 per cent carbon dioxide
× 35.2 liters of air leaving chamber (*A*)

0.177 liters carbon dioxide
+ 0.013 residual change (*D*)

0.190 liters of carbon dioxide produced by patient
÷ 2 minutes

0.095 liters of carbon dioxide produced per minute and measured at 739.3 mm. 21.7 degrees = 236 Gm. of carbon dioxide per twenty-four hours

236
× 2.967 calorific value of carbon dioxide at respiratory quotient of 0.83

701 calories per twenty-four hours
700 calories: normal for weight
865 calories: normal for age

This method of determination of the metabolism involves principles commonly in use in determining respiratory metabolism in adults and in animals. Making use of as short periods of observation as from two to four minutes, however, is somewhat unique. In practice it has been found much superior to other methods in use in our laboratory as to both the time required and the agreement of duplicate results.

The speed of the air current is varied according to the size of the child and is set at what seems the proper rate at the beginning of the period. This may be checked by passing air into the gasometer for a one minute period. The ventilation rate used is given approximately in the accompanying table.

Ventilation of Air Current as Varied by Size of Child

Weight of Child, Kg.	Rate of Air Current Liters Per Minute
5	8
10	12
15	18
20	24
25	30

The proper adjustment of the current of air greatly diminishes changes in the residual percentages of carbon dioxide in the box at the start and end of each period. In most of our determinations, the residual change in carbon dioxide in the box has been less than 10 per cent of the total carbon dioxide collected in the gasometer; when it has exceeded 15 per cent, the agreement of duplicate determinations has not been so satisfactory. However, it is obvious to those accustomed to determinations of respiratory metabolism in children that the activity of the child is a greater cause of variations than technical errors.

CELIAC DISEASE

A REPORT OF METABOLIC OBSERVATIONS ON FOUR CASES *

MARTHA VAN KIRK NELSON, M.S.
IOWA CITY

Observations on the progress of four small girls with celiac disease seem of sufficient interest to report, since normal growth and development were obtained and since certain fairly popular dietary measures were found to be of relatively little value.

From the nutritional standpoint celiac disease is characterized by an inability to utilize fats, starches and the more complex sugars. When these are fed a large proportion of the ingested food is lost through the feces, and as a consequence metabolic deficiencies result. On this basis can be explained much of the clinical picture of celiac disease, such as abdominal distention, peculiar character of the stools, retardation of growth and marked tendency to infections and dental caries.

The child suffering from celiac disease has the same nutritional requirements as the normal child, and attempts to eliminate the foods not tolerated have resulted frequently in diets lacking in some of the known essentials. Marked stunting and dental caries have prevailed in many cases even when the diet was such as to control the diarrhea. Standard textbooks advise a diet so restricted in quantity that growth is not to be expected.

It is the purpose of this report to record observations of some of the dietary measures commonly employed and to discuss a diet which was successful in producing normal growth and development.

Protein [1] milk is frequently the chief constituent of the celiac diet, and the use of bananas [2] in the dietary of the child suffering from celiac disease is common. The metabolic observations herein reported do not indicate any special usefulness of these two dietary constituents in the management of celiac disease.

PROTEIN MILK

The powdered protein milks on the market are fairly similar in composition, containing approximately 33 per cent protein, 25 per cent sugar and from 25 to 30 per cent fat. While they are called "protein milk" and "albumin milk," the only constituent which varies greatly from

* Submitted for publication, Aug. 20, 1929.

* From the Department of Pediatrics, College of Medicine, State University of Iowa.

1. Sauer, Louis W.: Celiac Disease, Am. J. Dis. Child. **29**:155 (Feb.) 1925.

2. Haas, Sidney V.: Value of the Banana in the Treatment of Celiac Disease, Am. J. Dis. Child. **28**:421 (Oct.) 1925.

powdered whole milk is the decreased percentage of sugar. My metabolic observations indicate that fat in the quantity found in protein milk is not desirable. When the children received protein milk the fecal analyses showed that a large proportion of the milk fat and calcium was excreted.

During one observation protein milk was the sole constituent of the diet of D. T., aged 3½ years (case 3). The amount fed was calculated according to Sauer,[1] and had a total energy value of 1,200 calories. The child took the milk willingly, but there was a steady loss of weight (from 13.95 to 12.9 Kg.) during the three weeks on this diet. An analysis of the feces for three consecutive days of the period showed that practically all (85 per cent) of the fat was excreted. The child also was losing calcium in excess of her intake.

Protein milk, liver, cottage cheese, dextrose and orange juice composed the diet of two other children. In one case there was a slight loss of weight, and in the other the weight remained practically stationary. Analyses of the fecal output of these children showed that a high percentage of the fat and calcium was excreted.

When these children received a low fat, low cellulose diet, as listed in table 2, which furnished the same number of calories as did the diets containing protein milk, there was a steady increase in weight, the fecal fat was negligible and there was adequate retention of calcium.

These observations are interpreted to indicate that fat in the amounts present in protein milk is not desirable because of the loss of fat and with it other materials (e. g., calcium) in the feces.

BANANAS

No adequate explanation has been offered for the efficacy of the banana in the celiac diet. The character of the carbohydrate and the enzyme which it contains each has been suggested as the valuable constituent. The ripe banana resembles other equally ripe fruits in that it contains invert sugar, starch, a small amount of protein and mineral salts. The chief points of difference are the character of the cellulose and the enzyme of the banana. If the enzyme were a factor the banana should be more effective raw than cooked, and for the same reason pineapple juice which contains a similar enzyme should prove useful.

The validity of this theory might be demonstrated by a decrease in the weight of the dried feces when this enzyme is present in the diet. An increased efficiency of digestion and absorption would tend to decrease the total fecal output. The results of such a study are given in table 1. Four children with celiac disease and two with no digestive disturbances received diets low in fat and cellulose, with bananas, cooked and raw, pineapple juice and orange juice as the only variables. Care was taken to feed only very ripe bananas. Several

methods of ripening were tried. Bananas were kept in a warm dark place and were exposed to sunlight and to ultraviolet irradiation. Even after the skins were entirely black and some portions of the banana had begun to deteriorate, a positive starch test could be obtained. The possibility of securing a starch-free banana is doubtful. The pineapple juice was freshly expressed from the ripe fruit.

In every instance the weight of the dried feces was greater when the child was receiving raw bananas than when cooked ones were fed, and the change from orange juice to pineapple juice made no appreciable difference in the weight of the dried stools. When stained with iodine, the feces showed evidence of the presence of much starch when bananas were fed. The results obtained from the children with celiac disease were similar to those of the other children. From these observations the enzyme theory would appear to be unfounded, and it is inferred

TABLE 1.—*Weight of Dried Stools for the Twenty-Four Hour Period (Averages for Three Consecutive Days) of Four Children with Celiac Disease and Two with no Digestive Disturbance* *

Patient	Diagnosis	Dry Weight of Stool, Gm. Diet I	Diet II	Diet III
V. W.	Celiac disease	32.3	26.5	27.2
D. T.	Celiac disease	40.8	30.6	29.5
M. L.	Celiac disease	30.4	25.5	25.9
D. W.	Celiac disease	38.4	31.8	32.5
K. C.	Phlyctenular conjunctivitis	26.2	20.2	18.8
D. S.	Latent syphilis	30.2	23.1	23.6
	Averages	33.05	26.4	26.2

* The diet varied only in the content of raw and cooked banana, orange and pineapple juice. The foods constant in all the diets were: liver, cottage cheese, egg white, skimmed milk, dextrose, tomato juice, beef juice and corn flakes. To this were added: diet I, orange juice and raw banana; diet II, orange juice and cooked banana; diet III, pineapple juice and cooked banana.

that any benefit to be derived from the banana may be dependent on the availability of the sugar, due, in part at least, to the softness of the cellulose.

DEXTROSE

While proteins apparently are well tolerated, it would not be practicable to give an amount great enough to supply the total energy requirement of the child with celiac disease. Fats are not satisfactorily absorbed. Carbohydrates, in some form, therefore, must be depended on to supply the greater portion of the total energy. Since my observations indicated that a large proportion of the ingested bananas was excreted, some other source of carbohydrate was sought. Any carbohydrate which remains in the intestinal tract for an appreciable length of time may undergo fermentation and increase the number of stools and the abdominal distention. As dextrose in dilute solutions has been found to be readily absorbed in conditions not celiac; an attempt was made to use this carbohydrate to replace all or a portion of the bananas.

All four of the children with celiac disease were given dextrose in constantly increasing amounts. An equivalent amount of carbohydrate (banana) was omitted from the diet, other factors remaining constant. The dextrose was given in the form of a 10 per cent solution flavored with orange juice. To facilitate absorption, from 100 to 200 cc. was given at hourly intervals between meals. Later a more concentrated solution (20 per cent) was used. As much as 200 Gm. of dextrose was given daily. When given in this form between feedings of solid food, no diarrhea developed and the weight gain was accelerated. The number and bulk of the stools were decreased.

Corn syrup was not a satisfactory substitute for dextrose until some improvement had been noted. Diarrhea was instigated by the substitution of corn syrup for dextrose in one case, and was controlled by

TABLE 2.—*A Typical Initial Celiac Diet and One Which Was Tolerated After Two Years of Improvement* *

Initial Diet	Amount	Later Diet	Amount
Boiled skim milk	28 oz.	Boiled whole milk	1 quart
Cottage cheese	1 oz.		1 oz.
Egg whites	2 or 3	Whole eggs	2
Sieved liver (daily)	1 oz.	Three times each week alternated with scraped beef, ground chicken or fish	1 oz.
Dextrose	6 oz.	Corn syrup	4 oz.
Baked bananas	1 or 2	Alternated with sieved stewed pear, peach, apricot, apple or orange pulp	3 oz.
Strained orange juice	8 oz.		3 oz.
Sieved tomato	8 oz.	Alternated with sieved peas, squash, string beans and carrots	6 oz.
		Corn flakes	1 oz.
		Well cooked rice	1 oz.
		Dextrinized toast	1 slice
	(Beef juice was given for additional iron)		

* The initial diet as given was for a child aged 2½ years, weighing 20 pounds (9 Kg.). The later diet was that of the same child two years later. In the case of other patients, the amounts fed were proportional to the age of the child.

reverting to the former diet. After several months, however, this substitution was made in each case with success.

COMMENT

The test for the adequacy of the diet for the child with celiac disease should not stop with control of the diarrhea. All of the essentials for growth and development of the normal child are necessary for the proper nutrition of the child with celiac disease. Clinical observations alone may be insufficient. Protein milk and bananas may seem adequate because the diarrhea and muscular wasting are checked, yet an analysis of the feces shows that excessive amounts of starch, fat and calcium are excreted.

The constituents of the diet which supplied the essentials in a form in which they could be utilized by my patients are listed in table 2. The protein content of the diet ranged between 1.5 and 2 Gm. per pound of theoretical weight. The energy value was that for full activity

as advised by Holt and Fales. The protein and minerals were supplied by skimmed milk, cottage cheese, egg white and liver, with an additional small amount of minerals in the vegetables and beef juice. The vitamins were supplied by cod liver oil (2 teaspoons daily), orange juice and tomato juice (from 10 to 15 ounces per day). Dextrose and small quantities of baked bananas provided additional energy. As improvement became evident other foods were added. Table 2 shows also a typical diet which has been tolerated after two years of gradual improvement.

Progress studies of each child indicated that the tolerance for a small amount of fat (egg yolk, whole milk) was regained before a tolerance for starches. After several months of satisfactory dietary control, the ingestion of starch, such as white crackers, produced a period of typical celiac diarrhea which lasted for five days. Attempts to add starches to the diet were unsuccessful even after whole milk and egg yolk were well tolerated.

Short summaries of each of the four cases are given. In every instance the adequacy of the diet has been demonstrated by normal growth and development of the child, an arrest of the tooth destruction so prevalent in celiac disease, and by the results of metabolic observations on the absorption of the ingested foods.

REPORT OF CASES

CASE 1.—*History.*—D. W., a girl, aged 3 years, was first observed in October, 1924. Her weight was 20 pounds (9 Kg.). There had been recurrent periods of diarrhea since birth. There had been noticeable enlargement of the abdomen since the age of 9 months. The dietary history was not obtained.

Examination.—The child appeared markedly undernourished and had extreme enlargement of the abdomen, the circumference of which was 55 cm. (fig. 1). She was fretful and pale, and a particularly distressed facial expression was noted. Dental examination revealed extensive active caries. Fecal analysis showed a fat excretion of 71 per cent of the intake, 50 per cent of which was excreted as fatty acids and soaps. Marked dilatation of the transverse and descending colon was evident from roentgen examinations.

Progress.—At first the patient received a high protein, high banana diet. Weight fluctuations continued although the diarrhea was decreased. The most rapid progress was made after the low fat, low cellulose diet was started. In April, 1929, the child was taking a normal diet for a child of her age and metabolic observations showed good digestion and absorption. The teeth were hard and free from active caries.

CASE 2.—*History.*—M. L., a girl, aged 2 years, was observed first in October, 1925. Her weight was 18½ pounds (8.4 Kg.).

She had a serious illness ten months previous to this observation, characterized by diarrhea, protuberant abdomen and excessive loss of weight. An inadequate dietary history was obtained.

Examination.—The child appeared fairly well nourished but the enlargement of the abdomen was striking. The stools were pasty and gray, and in size were

out of proportion to the intake. The quantity of fat excreted was 90 per cent of the amount ingested, 80 per cent of which was present as split fat.

Progress.—Improvement was rapid on a low fat, low residue diet. In November, 1928, she appeared as a normal child. The teeth were hard and free from caries. A diet containing a moderate amount of fat and starches was permitted at this time and metabolic studies showed adequate digestion and absorption.

CASE 3.—*History.*—D. T., a girl, aged 3 years, was observed first in November, 1925. Her weight was 17 pounds (7.7 Kg.). Diarrhea had begun at the age of 13 months and had been present intermittently since that time. Gradual enlargement of the abdomen and extreme muscular wasting had developed concurrently. No adequate feeding history was obtained, except that little milk had been taken since the child was 1 year old.

Fig. 1 (case 1).—Condition in 1925, and two years later.

Examination.—The child appeared listless and too weak to stand (fig. 2). There were marked bowing of the humeri and femora and massive destruction of the teeth. The gums were swollen and tender. The abdomen was protuberant, with no evidence of fluid or palpable masses. Roentgenograms showed healing scurvy and active rickets. A gastric and colon series revealed an enormous atonic stomach, and dilatation and atony of the colon. The stools were foul, grayish and in size were out of proportion to the food intake. No analysis of feces was made when the patient was first seen. Later studies, with the patient on a diet containing 15 Gm. of fat, showed an excretion of 8 Gm., 72 per cent as fatty acids and soaps and 28 per cent as neutral fat.

Course.—The course was especially stormy for several months. Large, foul, grayish stools persisted until a low fat, low cellulose diet was instituted. At the time of writing, the child was well and attended school. Measurements of height and weight showed a normal development for her age and the teeth were hard and

free from active caries. Metabolic studies revealed an increased tolerance for fat, but still some inability to tolerate starch.

CASE 4.—*History.*—V. W., a girl, aged 2½ years, was observed first in April, 1926. Her weight was 22½ pounds (10.2 Kg.), but there was edema of the feet and legs. In January, 1926, the child was severely ill with diarrhea and showed marked loss of weight. There was progressive loss of appetite, with some vomiting, and the abdomen became noticeably enlarged. The diet had consisted chiefly of meat and potatoes, with few vegetables and no cod liver oil, eggs or fruits. Practically no milk had been taken since the age of 1 year.

Fig. 2 (case 3).—Condition in 1924, and three years later.

Examination.—The child appeared malnourished with an extremely prominent abdomen, the circumference of which was 56 cm. This was associated with edema of the feet and legs, marked pallor and a distressed facial expression. The teeth appeared normal. An examination of the feces revealed 60 per cent excretion of ingested fat; 86 per cent of this was present as split fat. Dilatation and atony of the sigmoid and descending colon were evident from roentgen studies.

Progress.—Improvement was inhibited at the beginning by many infections—tonsillitis, mastoiditis, measles and chickenpox. Response to the low fat, low residue diet was satisfactory. When this child was last seen in May, 1928, she was apparently in excellent health and had grown normally for a child of her age.

No dental caries had developed. Fats such as egg yolk and whole milk were well tolerated. An attempt to add bread and potatoes at this time was followed by a period of diarrhea.

SUMMARY

1. The successful feeding of four children with celiac disease is reported. Adequate utilization of food was demonstrated by normal growth, arrest of dental caries and the results obtained from metabolic studies.

2. Protein milk was found to be inadequate due to the increased fat and calcium output.

3. Proteins such as boiled skimmed milk, cottage cheese, egg white and sieved liver were well tolerated.

4. The enzyme theory concerning the efficacy of the banana was not substantiated. Whatever value the banana has in the treatment for celiac disease apparently is dependent on the availability of the sugar; this is probably due, in part at least, to the softness of the cellulose.

5. When given between meals, dextrose was tolerated in relatively large amounts and permitted an adequate energy intake.

INTERNAL HEMORRHAGIC PACHYMENINGITIS IN YOUNG CHILDREN

A REPORT OF SIX CASES *

FRED C. HUNT, M.D.
NEW YORK

Despite the fact that internal hemorrhagic pachymeningitis is not uncommon during infancy, there are few cases reported in the literature. Moreover, comparatively few have been followed over prolonged periods of time, so that observations as to sequelae are incomplete. Recovery following the initial lesion is usual, although Burhans and Gerstenberger [1] found that many of these infants later showed a permanent disability. Feer [2] and Finkelstein [3] expressed the belief that hydrocephalus was the most frequent sequel. Rosenberg [4] was able to locate a few of his patients eight or nine years after the first appearance of the disease and found that 70 per cent had some defect directly traceable to the original lesion.

Virchow,[5] who first described the condition, believed that the primary lesion was a proliferation of subendothelial tissue followed by serofibrinous exudate and hemorrhage. This view was also supported by Heschl [6] among the earlier writers. On the other hand, Wiglesworth [7] considered hemorrhage to be the primary lesion. Doehle,[8] as well as Burhans and Gerstenberger, believed that the formation of

* Submitted for publication, Sept. 18, 1929.

* From the Department of Pediatrics, Cornell University Medical College, and the New York Nursery and Child's Hospital.

1. Burhans, C. W., and Gerstenberger, H. J.: Internal Hemorrhagic Pachymeningitis in Infancy, J. A. M. A. **80**:604 (March 3) 1923.

2. Feer, E.: The Diagnosis of Children's Diseases (Translated by Scherer), ed. 2, Philadelphia, J. B. Lippincott Company, p. 486.

3. Finkelstein, H.: Lehrbuch der Säuglingskrankheiten, Berlin, Julius Springer, 1924, p. 520.

4. Rosenberg, O.: Die Pachymeningitis haemorrhagica interna im Kindesalter, Berl. klin. Wchnschr. **50**:2272, 1913.

5. Virchow, von R.: Das Hämotom der Dura Mater, Verhandl. d. phys.-med. Gesellsch. zu Würzb. **7**:134, 1857.

6. Heschl, R.: Compendium der pathologischen Anatomie, Wien, Wilhelm Braumüller, 1855.

7. Wiglesworth, J.: Remarks on the Pathology of So-Called Pachymeningitis Interna Haemorrhagica, Brain **15**:431, 1892.

8. Doehle: Ueber chronische Pachymeningitis bei Kindern und deren forensische Bedeutung, Verhandl. d. X Internat. Med. Cong., V (Gerichtliche Medicin), Aug. 8, 1890, p. 40.

the subdural membrane was secondary to a meningeal hemorrhage occurring at birth; but evidence for this view is inconclusive. Schwartz,[9] Finkelstein,[10] Feer,[11] Gordon [12] and most recent authors agreed with the original view of Virchow. In support of this belief, that the hemorrhage is secondary, is the case cited by Gordon, in which subdural proliferation was present without evidence of bleeding. The acute onset of severe symptoms is ascribed to the suddenly increased intracranial pressure resulting from the hemorrhage.

Herter [13] reported two cases of his own and quoted from fifty-seven others. Rosenberg pointed out that in practically all of the reported cases the patients had been artificially fed and had led an institutional life. In some of these patients there had been a diphtheric nasal infection, and he advanced the belief that a cavernous sinus thrombosis with venous congestion and meningeal hemorrhage was the etiologic agent. This explanation has received little support from other authors.

REPORT OF CASES

In five of the six cases to be reported, the children were boys. The first symptoms appeared before the age of 10 months. A diagnosis was made in each case by obtaining a xanthochromic fluid, containing red blood cells, from the subdural space. Retinal hemorrhages were observed in five cases, and the other infant showed a distinct papilledema. Wassermann reactions of the blood and spinal fluid were repeatedly negative. Intracutaneous tuberculin tests (0.2 mg.) were likewise negative. One infant had a pronounced secondary anemia with an otherwise normal blood picture. Urinalysis showed no abnormalities.

Five of the children have been under constant observation for from one to five years. The sixth infant died during the acute stage of the disease, and the diagnosis was confirmed at postmortem examination.

CASE 1.—R. T. was born on Feb. 7, 1924, of a mentally retarded unmarried mother. He was well until 3 months when an intestinal upset necessitated hospital care. Convalescence was rapid, and no physical or mental abnormality was noted at that time.

In July, 1924, the child was beginning to sit up and seemed well advanced for his age. During the latter part of this month, however, he had two unexplained convulsions and was brought to the hospital for observation. Lumbar puncture gave

9. Schwartz, A. B.: The Etiology of Pachymeningitis Hemorrhagica Interna in Infants, Am. J. Dis. Child. **11**:23 (Jan.) 1916.

10. Finkelstein, H.: Ueber Pachymeningitis Hermorrhagica im Kindesalter, Jahrb. f. Kinderh. **74**:451, 1911.

11. Feer, E.: Cor.-Bl. f. schweiz. Aerzte **45**:598, 1915.

12. Gordon, A.: Internal Pachymeningitis in Young Children, New York M. J. **99**:720 (April 11) 1914.

13. Herter, C. A.: Hemorrhagic Internal Pachymeningitis in Children, Am. J. M. Sc. **116**:202, 1898.

a normal fluid, under increased pressure. Ophthalmoscopic examination showed scattered, small, retinal hemorrhages. A subdural puncture gave a xanthochromic fluid, showing microscopically many red blood cells. There were no further convulsions, and he was discharged at the end of six weeks.

The following six months were typically those of a quiescent period. Mental and physical development was at a standstill. Following this stage, however, the child improved rapidly, so that by July, 1925, at the age of 17 months, he was able to stand unsupported, recognized objects and seemed playful. The circumference of the skull was then 51 cm., and the anterior fontanel was nearly closed.

During the latter part of the second year, his mental development ceased. He refused to stand, became unresponsive and dull but showed no evidence of further subdural hemorrhage.

Following this second period of arrested development his progress was slow. At 3 years, a bilateral internal strabismus first became evident, and he has since worn glasses with little improvement. The eyegrounds were normal on examination. He did not speak until the age of 3½ years and had little initiative. At 4 years, deformities of the feet developed. Marked pronation and a calcaneovalgus deformity required special orthopedic shoes, and for the past year (June, 1928, to July, 1929) he had regularly attended a gymnastic, orthopedic clinic without improvement. He remained untrained in his habits until 5 years. A psychometric test at that time showed a mental age of 3 years and 6 months and an intelligence quotient of 70 per cent.

At the last examination (July 16, 1929) the following sequelae were present: bilateral internal strabismus, bilateral calcaneovalgus with marked pronation and mental retardation.

CASE 2.—L. F. was born on Oct. 2, 1924, after a prolonged labor ending in an instrumental delivery. At 4 months he had bronchopneumonia accompanied by gastro-intestinal intoxication with dehydration. Recovery was rapid and uneventful.

At 7 months, an enlargement of the head was noted which increased rapidly during a period of three weeks. He was admitted to the hospital for observation. Examination showed a wide separation of the cranial sutures. The anterior fontanel measured 10 cm. in its transverse diameter and the posterior fontanel was open. The circumference of the skull was 47 cm. A bilateral internal strabismus was present and retinoscopy showed a moderate papilledema, but no hemorrhages. Lumbar puncture was negative, on two occasions, except that the fluid was under increased pressure. Blood containing cerebrospinal fluid was obtained in two subdural punctures on successive days. Fluid withdrawn from the left lateral ventricle was yellow, but it contained no red blood cells. The eyegrounds continued to show a moderate papilledema but no hemorrhages.

During the following year (1925) his progress was disappointing. At the age of 14 months he made no attempt to stand or crawl. The lower extremities were flaccid to an extreme degree. The gluteal muscles showed wasting. The cranial circumference remained 47 cm.

At the age of 20 months he began to crawl, but it was not until 3½ years that he began to walk, even with assistance. His legs showed a genu valgum deformity and there was pronation of the feet. He had not yet learned to speak. The anterior fontanel measured 3 cm. in its transverse diameter, and the circumference of the head was 51 cm. His height was only 29 inches (73.66 cm.) as compared with the normal average of 38 inches (96.44 cm.) for a child of this age.

Because of urinary retention and distention of the bladder cystoscopy was performed, but no anomaly of the urinary tract was found. The bladder was palpable well above the umbilicus, and there was constant urinary overflow.

During the fifth year his mental status showed slight improvement. He began to talk but formed only short sentences. The deformity of his feet improved, but the genu valgum persisted. The strabismus disappeared, and ophthalmoscopic examination revealed normal fundi. He was still untrained in his habits and apparently had little control of urethral or anal sphincters. His mental and physical development was that of an infant of 18 months. Two psychometric tests attempted in the past year were unsatisfactory.

When last seen at the age of 4¼ years, he was a dwarfed, mentally retarded child. The anterior fontanel was still open and the cranial circumference was 51 cm. His height was 34 inches (86 cm.) and his weight 31 pounds (14.1 Kg.). Genu valgum and bilateral pes planus were present. The musculature of the bladder was atonic and the sphincter control incomplete.

CASE 3.—W. H. was delivered normally on March 27, 1925, and entered the hospital two weeks later for regulation of feeding. Examination gave negative results.

Fig. 1.—W. C., aged 21 months (left) shows no sequelae. L. F., aged 4½ years (right) shows dwarfism, poor muscle development and deformities of the lower extremities.

Three generalized convulsions, within a period of five days, occurred at the age of 10 months, and for this reason he was again admitted to the hospital. The circumference of the head was 47 cm. and the frontal bosses were prominent. No evidence of tetany was present. An analysis of the blood showed normal figures for serum calcium (9.3 mg. per hundred cubic centimeters of blood). Lumbar puncture yielded a normal fluid. He was discharged with a diagnosis of convulsions of undetermined origin. Three days later he was found in a state of coma and could not be roused for four hours, at which time he was readmitted to the hospital. Examination showed a bulging anterior fontanel, and retinoscopy revealed many small hemorrhages along the margins of the vessels and one free clot in the vitreous humor. A subdural tap gave a xanthochromic fluid under increased pressure with many red blood cells. There were no further convulsions.

During the second year, his mental development remained stationary. He was unfriendly, cried at the approach of strangers, showed no tendency to play with other children and appeared dull and listless.

He was 2 years old before he attempted to stand. Temper tantrums were frequent, and he cried when left alone. Six months later, at the age of 2½ years, he began to talk and his disposition improved. He then weighed 27 pounds (12.2 Kg.) and was 34 inches tall. His habits were not yet formed.

When 4 years old he was able to join a few words together to form short sentences. A slight exophthalmos was noted but the eyegrounds were normal. A psychometric test gave an intelligence quotient of 91.3 per cent. His mental status was decidedly improved over that of the previous year.

Recent examination (July, 1929) showed a mild degree of hydrocephalus, some exophthalmos and slight mental retardation.

CASE 4.—W. C., a foundling, whose estimated birthday was Sept. 22, 1927, was first seen at the age of 6 weeks because of a mild nasopharyngitis. Results of examination were otherwise negative.

At the age of 6 months he had three convulsions. A general physical and neurologic examination, including lumbar puncture, was negative. The only

Fig. 2 (case 5).—D. R., aged 14 months. Note the hydrocephalus and generally poor muscular development.

abnormal observation was a cranial circumference of 44.5 cm. as compared with a chest measurement of 40 cm. Two weeks later, while still in the ward under observation, there occurred, without apparent cause, a large ecchymosis about the left eye, involving both lids and the bulbar conjunctiva. Retinal hemorrhages were seen on ophthalmoscopic examination.

Subdural puncture yielded a xanthochromic fluid containing red blood cells. There were no further convulsions and the patient was discharged.

An examination of the eyegrounds two months later still showed the presence of retinal hemorrhages. The skull still measured 44.5 cm. in circumference.

At 1 year, he showed no neurologic abnormalities. There was no muscle atrophy. The fundi were normal. He was able to stand alone and played well. The fontanel was nearly closed and the head was normal in size.

Final examination, made when he was 22 months, showed a physically small but normal infant. His height was 31 inches (78.74 cm.) and his weight, 22 pounds (10 Kg.). The fontanels were closed. He walked alone and talked moderately well, comparing favorably with normal children of the same age.

CASE 5.—D. R., whose birth on May 28, 1928, was uneventful, first came under observation at the age of 4 weeks for regulation of feeding and treatment for thrush. At this time a slight, general hypertonicity was observed, and two weeks later vomiting, which was uncontrolled by atropine, manifested itself.

Despite the vomiting he continued to gain weight. An anemia manifested by a red blood count of 2,810,000 with 9.1 Gm. of hemoglobin responded well to a blood transfusion and oral administration of iron ammonium citrate. On discharge the red cell count was 4,130,000, and the hemoglobin, 10.8 Gm. per hundred cubic centimeters. He began to sit up, with support, at 6 months, and although vomiting persisted once or twice daily, his progress was good.

At 10 months, a rapid increase in the size of the head accompanied by more severe vomiting and diarrhea necessitated hospitalization. The head appeared abnormally large because of small body development, being 46 cm. in circum-

Summary of Data in Six Cases

Case	Age at Onset, Months	Early Symptoms	Duration of Observation Following Diagnosis	Sequelae
R. T.	5	Convulsions.....	5 years	Mild hydrocephalus; calcaneo-valgus; pronation; bilateral internal strabismus and visionary defect; mental retardation
L. F.	7	Rapidly enlarging head with separation of cranial sutures; Bilateral internal strabismus	4¼ years	Stunted growth; mental retardation; genu valgum; calcaneo-valgus; atrophic bladder; incontinence of urine and feces; open fontanel
W. H.	10	Convulsions; coma.....	3½years	Hydrocephalus; mild exophthalmos
W. C.	6	Convulsions; enlarging head and widely separted sutures; conjunctival hemorrhage	15 months	None yet evident
D. R.	10	Vomiting (began at 6 weeks); rapidly enlarging head; lassitude; frequent yawning; regression of mental development	4 months	Hydrocephalus; mental retardation
D. B.	5	Convulsions; coma.....	3 days	Died

ference as against a circumference of the chest of 40 cm. His length was 27 inches (68.56 cm.). Lumbar and subdural taps and ophthalmoscopic examination were all negative. He was discharged at the end of two weeks with a provisional diagnosis of chronic hydrocephalus, cause unknown.

He was readmitted the following week because of lassitude, refusal to sit up—as he previously had done—frequent yawning and vomiting. Examination of the fundi now showed papilledema and a small hemorrhage into the left retina. A subdural puncture yielded a xanthochromic fluid under pressure. There were numerous red blood cells, seen microscopically, in this fluid. A spinal puncture was negative. The circumference of the head was 47.3 cm.

During the next month the child seemed content to remain quietly in his crib, making no attempt to sit up, and cried but little. He took the bottle well, but otherwise seemed uninterested in his surroundings. Following this quiescent stage there was rapid improvement. Within two weeks he began to creep, said single words, became playful and happy and gained 2 pounds (5 Kg.).

He was apparently normal except for a mild hydrocephalus when examined in July, 1929.

CASE 6.—D. B., a colored girl, aged 5 months, was admitted to the hospital because of repeated convulsions of two days' duration. Except for three generalized convulsions one month previous to admission, the past history was negative. Examination showed a rachitic infant in coma. The anterior fontanel was tense, but there was no other sign of meningeal irritation. A to-and-fro systolic murmur was heard at the base of the heart. The blood serum calcium was 7.6 mg., and the organic phosphorus, 4 mg. per hundred cubic centimeters. A diagnosis of tetany was made, and therapeutic doses of calcium and ammonium chloride were given.

The infant did not respond to treatment and the convulsions continued. An ophthalmoscopic examination on the day following admission showed multiple hemorrhages in all layers of the right retina. An unsuccessful attempt was made to obtain fluid from the subdural space. The child died on the third day following admission.

Postmortem examination revealed a considerable quantity of partially clotted blood between the dura and the pia-arachnoid over the left parietal lobe. A smaller quantity, similarly placed, occupied the right side. These clots were loosely adherent to the dura, which was thickened and edematous. There were antemortem thrombi in the veins emptying into the superior longitudinal sinus and a thrombosis of the central vein of the right retina. The cavernous sinus was free from clots. The heart showed a patent ductus arteriosus.

SUMMARY

Six cases of internal hemorrhagic pachymeningitis in young infants are reported. These cases show the appearance of sequelae as late as three or four years following the initial lesion.

Following the acute, early symptoms, which may be severe enough to cause death, there is a quiescent period. During this time there may be regression, or at the best, a cessation of mental and physical development. This is followed by a period of rapid, almost phenomenal progress, but still later the sequelae appear.

The sequelae observed in these cases were hydrocephalus, mental retardation, visionary defects, muscular weakness causing chiefly deformities of the lower extremities, disturbances of the bladder and behavior problems.

161 West Sixty-First Street

INTERPRETATION OF ROENTGENOGRAMS OF THE CHEST IN CHILDREN BASED ON OBSERVATIONS AT NECROPSY

III. DISEASES OF THE LUNGS, OF THE PLEURA AND OF THE MEDIASTINUM *

JOHN A. BIGLER, M.D.
CHICAGO

This study was undertaken for the purpose of ascertaining what pathologic changes were present in the lungs of children to account for shadows in the roentgenograms of the chest.

In previous papers,[1] the normal chest, the hilar shadows and the linear markings and tuberculosis were discussed. In this paper, observations in bronchopneumonia and lobar pneumonia and diseases of the pleura and of the mediastinum will be considered.

PNEUMONIA

In young children, lobar pneumonia occurs less frequently than bronchopneumonia, and fewer cases come to necropsy because it is less fatal. The picture of a dense homogeneous shadow involving one lobe or part of one lobe, with fairly sharp borders, is easily recognized. There is no displacement of the trachea, mediastinum or heart. In a few instances when lobar pneumonia had been diagnosed before death, a massive bronchopneumonia, pseudolobar in character, was found.

The areas of involvement in bronchopneumonia were small, generalized and sharply defined patches of increased density on the film (fig. 1) in only two instances. In one there was bilateral involvement, while in the other the involvement was unilateral. Both resembled rather closely the observations in miliary tuberculosis of the lungs. In all the other cases the shadows on the film were of increased density, but had no lobar distribution. They were not discrete, so that they gave rather large areas of the pulmonary fields an appearance of increased density with considerable mottling and with an increase of linear markings into the involved regions (fig. 2).

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* From the Children's Memorial Hospital and the Otho S. A. Sprague Memorial Institute Laboratory.

1. Bigler, J. A.: Interpretation of Roentgenograms of the Chest in Children Based on Observations at Necropsy: I. The Hilar Shadows and the Linear Markings, Am. J. Dis. Child. **38**:978 (Nov.) 1929; II. Tuberculosis, ibid. **38**:1166 (Dec.) 1929.

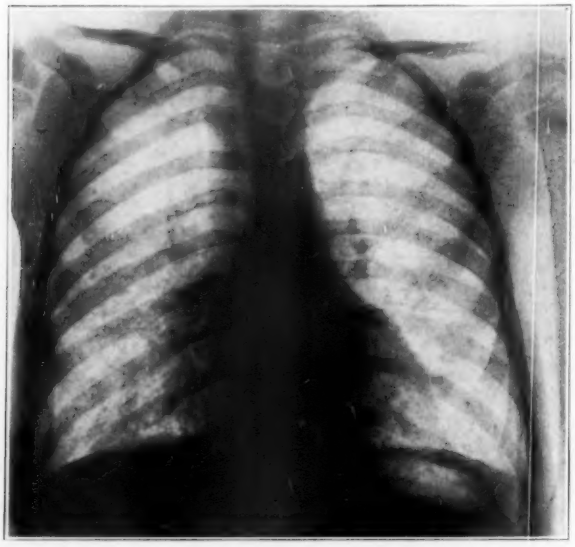

Fig. 1.—The fine mottling shadows are due to bilateral bronchopneumonia.

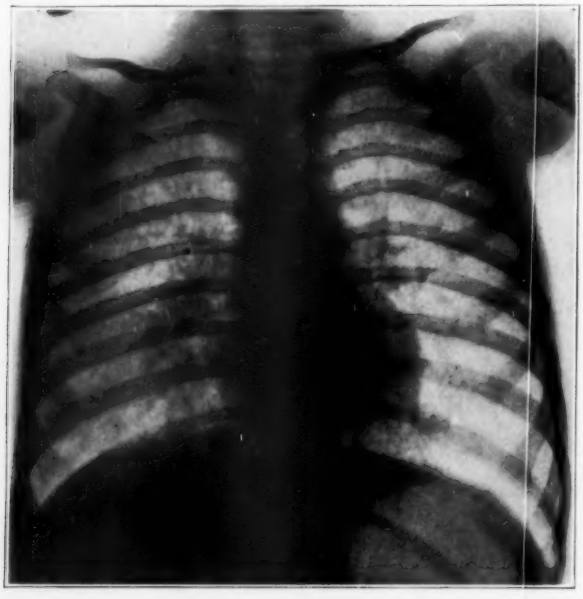

Fig. 2.—Bronchopneumonia of the right lung, with a common type of shadow; prominent linear markings of the left lung.

Pathologically, pleural involvement in bronchopneumonia was not as common as in lobar pneumonia. In the majority of cases the pleurae remained smooth and shiny, or at the most were only slightly dull.

COLLAPSE OF THE LUNG

In collapse of the lung there may be involvement of the whole lung, one lobe or part of one lobe. In some instances there may be more than one area of collapse. The condition is usually due to the plugging of a bronchus with mucus or with some other type of foreign

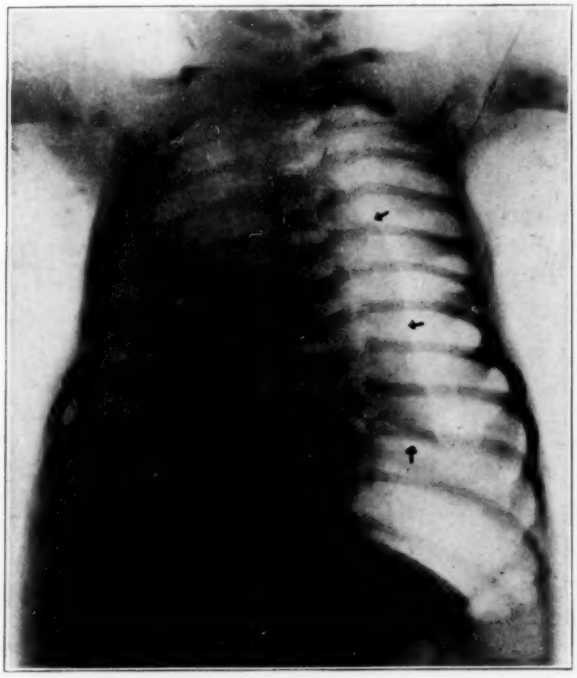

Fig. 3.—Left pneumothorax with collapse of the lung following an intracardiac puncture.

body. As long as the bronchus is not completely plugged, so that air can pass both ways, there need be no roentgenographic observations. A foreign body itself will not be discernible unless it is opaque to the rays. Early in the condition, no roentgenographic observations may be obtainable, but if the air is absorbed from the lung distal to the plugged bronchus, the lung collapses and shows on the film as an area of increased density in contrast to the aerated part. As the lung collapses, however, owing to its loss of air, certain other events must happen. The pleural cavities are closed cavities in which the pressure is slightly less than atmospheric. For this reason, as the lung collapses it cannot fall

away from the chest wall because that would further decrease the pressure. To compensate for this, the heart and mediastinum, which normally are movable, are pulled to the involved side, and there is often a pulling in of the chest wall and a raising of the diaphragm. If there is a collapse of the lung from the chest wall, there must be some other condition present, such as a hydrothorax, a pneumothorax or some form of the two conditions (figs. 3 and 7). In a simple collapse of the lung there is no empty space between the lung itself and the chest wall.

ASTHMA AND EMPHYSEMA

In my little experience with asthma and emphysema, I have obtained no distinctive roentgenographic observations in children. The conditions are easier to recognize by fluoroscopic examination. In the film there may be some evident flattening of the diaphragm, and the chest may appear somewhat lighter than normal with the linear markings extending fairly well to the periphery. The ribs may also flare out at a greater angle than is seen normally. I have noted in the postmortem examination of these children that the anterior medial margins of the lungs are markedly aerated and encroach as far as possible anteriorly over the mediastinum, so that they almost reach the midline under the sternum. In checking these cases with films, it was frequently seen that over the mediastinum there was a large area of decreased density which extended inward from the normal pulmonary field. Most often this was present bilaterally, but occasionally only unilaterally. In some cases it gave the left upper border of the heart a sharply oblique, cutoff appearance.

CONGENITAL LARYNGEAL STRIDOR

In two cases of congenital laryngeal stridor there were no roentgenographic observations other than those of emphysema.

DISEASE OF THE PLEURA

Pleural disease does not often appear as a primary infection in children, but as a secondary condition to pulmonary disease it is important because of its frequent occurrence. Pathologically, two general divisions can be made of secondary pleural disease as it applies to roentgenographic observations, namely: (1) disease of the pleura without fluid and (2) disease of the pleura with fluid.

In the first general classification can be put all cases of thickening of the pleura and of pleural adhesions. Pleural thickening may be fibrous or it may be due to a thick, shaggy, fibrinopurulent exudate. It may be generalized, involving one or both lungs, or localized in one lobe or in any part of it. The thickened pleurae that were seen

followed empyema, pyopneumothorax, tuberculosis or pneumonia with a marked fibrinous pleuritis. On the film these were usually seen as areas of increased density with faint lung markings. When seen along the lateral chest wall, they were in evidence as a shadow of varying width with a straight medial border, indicating that the aerating lung did not extend to the lateral chest wall (fig. 4). When lying over the pulmonary field, the borders were usually irregular and gradually shaded off into normal-appearing pulmonary shadows. At times one of the borders might be sharp and might correspond with the position of the interlobar fissure, especially on the right side. When serial roent-

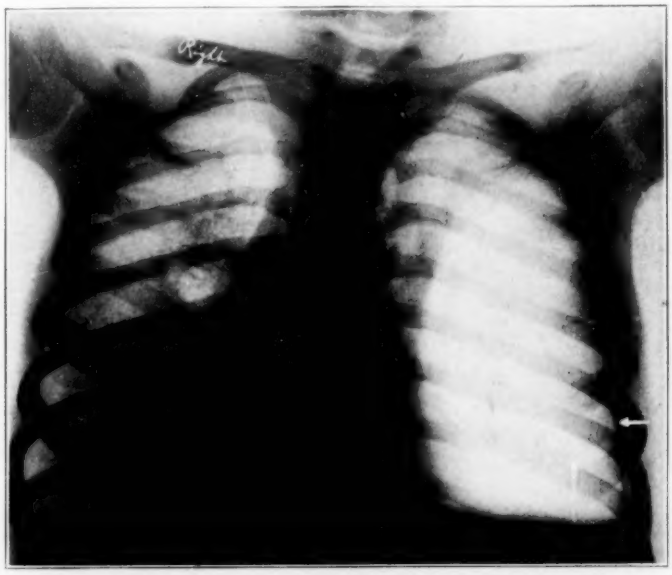

Fig. 4.—Left pyopneumothorax with the fluid level at the base of the lung. Increased density of the left apex due to the thickened pleura over the aerating part of the upper lobe. The shadow in the right lower lobe is due to an encapsulated empyema, although the borders of the shadow are not clearly defined. The arrow indicates a shadow along the lateral chest wall due to the thickened parietal pleura.

genograms were obtained, this density was seen to disappear gradually in the majority of cases, leaving a normal-appearing chest.

Pathologically, pleural adhesions were common, especially after infancy. The adhesions were usually fine, localized, fibrous strands between the visceral and parietal pleurae with little thickening of the pleurae themselves. They were not often shown on the film.

The finding of an interlobar line on films was a frequent occurrence, especially in younger infants. Often it was present on one film and not on a succeeding film. At times, there was evidence of other con-

ditions in the chest. The interlobar line was always present only on the right side (fig. 5). Often it extended straight out from the hilum to the lateral chest wall as a fine stringlike shadow. At times, this shadow was broad, and again, the medial portion was several times broader than its more lateral part. Often it curved gently downward from the hilum to the lateral chest wall, or only its outermost portion was curved. Occasionally it was curved slightly upward. When this shadow was checked pathologically, it was found to vary in position and extent according to the location, shape and size of the middle lobe and according to the size of the interlobar fissure. In younger children there

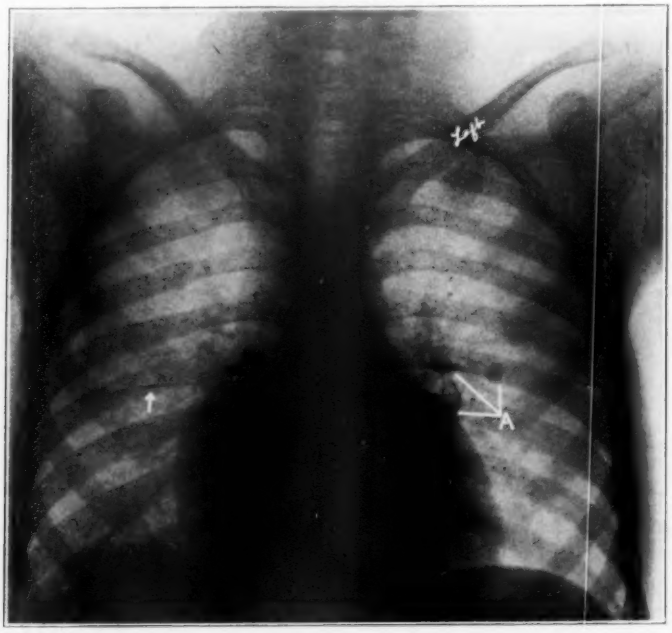

Fig. 5.—The arrow indicates the right interlobar pleural line; *A*, areas of calcification.

most frequently was no change in the interlobar pleura in the cases with an inconstant-appearing shadow, but in older children there was practically always a thickening of the interlobar pleurae with adhesions between the adjacent layers. It was also found that the sharpness of the shadow and its thickness varied as to the point at which the target was centered on the chest. Interlobar lines were no more frequent in children who showed evidence of tuberculosis than in those who had had other types of pulmonary involvement.

Fluid in the pleural cavity may be purulent or nonpurulent. From the film alone it was rarely possible to tell what type of fluid was

present. If present bilaterally and involving all of both chest cavities, it was likely to be a transudate. Shadows due to fluid were usually homogeneous, and the degree of density depended not only on the thickness of the fluid, but more on the amount present. Small collections might be present in the form of an encapsulated empyema, or part or all of one pleural cavity might be filled. The borders outlining the extent of the fluid shadow were usually smooth and, if only part of the chest cavity was filled, the upper border or level often had an oblique course, being highest in the lateral part of the chest (fig. 6). There was practically always a complete loss of lung markings and the outline of the ribs on the affected side was diminished. This homogeneous

Fig. 6.—Empyema with an oblique upper border at the right side of the chest. No change is demonstrable in the fluid level.

shadow was often hard to differentiate from a pneumonic consolidation. In large pleural effusions, the heart, mediastinum and trachea were always pushed to the opposite side and there was a widening of the intercostal spaces on the involved side as well as a lowering of the liver shadow that was not found in pulmonary consolidations.

Early the fluid, as it collected at the base and along the lateral chest wall, seemed to float the lung or push it medially so that a definite line could be seen demarcating the pulmonary border. Lateral to this line, there was a homogeneous shadow of increased density with a complete absence of any lung markings. Medial to the line, the lung areas were of a density denoting the presence of aerating tissue and with evident

lung markings (fig. 7). There was rarely much displacement of the heart or of the medistinum at this stage. This type of shadow was found not only in early empyema, but commonly in pleural effusion due to cardiac decompensation. In empyema, as the amount of fluid increased and as it became thickened, this lateral line of the compressed lung disappeared, but often reappeared again as the fluid decreased in amount and the lung began to expand out from the hilum. Not only were these shadows checked by postmortem examination, but the presence of the fluid was also proved by aspiration in numerous cases.

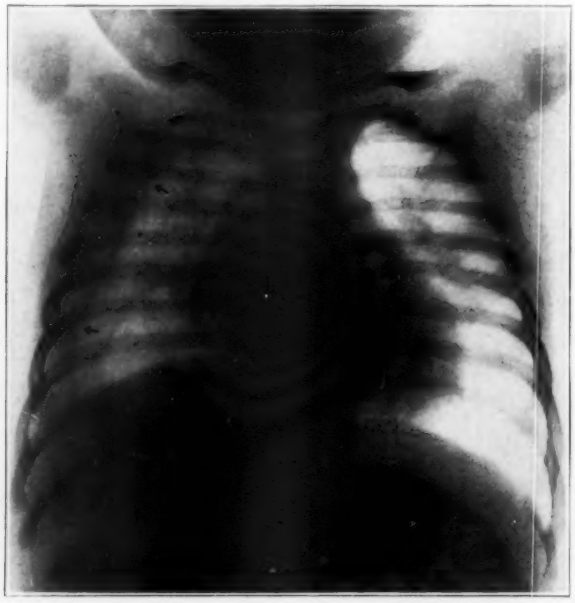

Fig. 7.—Early empyema of the right side of the chest, with the lung pushed from the chest wall by the fluid.

As the fluid decreased in amount, whether due to repeated aspirations, absorption or operation, the shadow always began to clear superiorly and medially. The last part to clear was the most lateral portion. During this stage there was often a beginning contraction of the chest wall with narrowed intercostal spaces on the affected side, the degree of which depended on the amount of fixation of the heart and mediastinum.

In no case of simple pleural effusion was it possible to demonstrate a change in the level of the fluid by a change in the position of the patient. Pleurisy with effusion due to tuberculosis was rare, both clinically and at postmortem examinations.

Two patients were examined post mortem, several years after they had recovered from an open operation for empyema. There were many fine, fibrous adhesions binding the parietal and visceral pleurae together on the involved side, but there was practically no thickening of the pleural leaves themselves, and no roentgenographic evidence of the previous condition except an exostosis of the ribs at the site of drainage.

I had no experience with interlobar encapsulated effusions. The roentgenogram was of the utmost importance in diagnosing pyopneumothorax, and often pointed the way when physical examination was inconclusive. In all patients in whom the presence of fluid was suspected the roentgenograms were taken with the patients in both the prone and the upright positions. The film showed the characteristic of a fluid level that always changed with the position of the patient and that was never found unless air was present. The bubble of air occurring with loss of lung markings varied in size and shape with the amount of fluid present and with the adhesions which often limited the size of the involved area (fig. 4). There was a displacement of the heart and mediastinum to the opposite side and, if the bubble of air was large enough, the shadow of the collapsed lung could be made out as an area of increased density near the hilum or the mediastinum. A rupture of the lung was found at necropsy in each instance, but it could never be demonstrated on the film. In one postmortem examination a small section of the lung was found bound to the lateral wall of the chest by adhesions while the rest of the lung was collapsed, leaving this thin flap, not more than one-fourth inch in thickness, stretched across the chest and casting on the film a shadow of even density. During the past year I was able to follow clinically in infants and young children about ten cases of pyopneumothorax that ended in complete recovery.

Simple pneumothorax in children was not rare. In a patient who came to necropsy, a pneumothorax was found that had not been present on the antemortem films. The patient's heart apparently stopped beating. One of the interns gave an intracardiac injection of epinephrine, which did not revive the heart. A few minutes later, respirations ceased. The postmortem film of the chest revealed a pneumothorax with collapse of the lung on the left side (fig. 3). Necropsy gave the explanation. When an attempt was made to inflate the lungs under water, the air kept bubbling out of two pinpoint holes through the anterior flap of the left upper lobe. The needle had penetrated two small bronchioles just beneath the pleura, and respirations had continued long enough to cause the pneumothorax. In another patient an intracardiac puncture was performed after death. At necropsy it was impossible to inflate the lung because, again, two small bronchioles had been punctured. No pneumothorax was found, as respirations had ceased before the puncture.

The incident showed, however, the ease with which a penumothorax, whether localized or of the whole chest cavity, could be produced in tapping the chest for either diagnostic or therapeutic reasons. The observations were the same as those for pyopneumothorax except that there was no fluid level present, and no increased density due to fluid.

I was able to follow clinically several children with localized pneumothoraces that developed spontaneously during the course of bronchopneumonia. They were followed closely with a long series of films. At the time of writing all have completely absorbed but one, which has remained the same size for several months (fig. 8). The shadows started as oval areas of decreased density with a complete

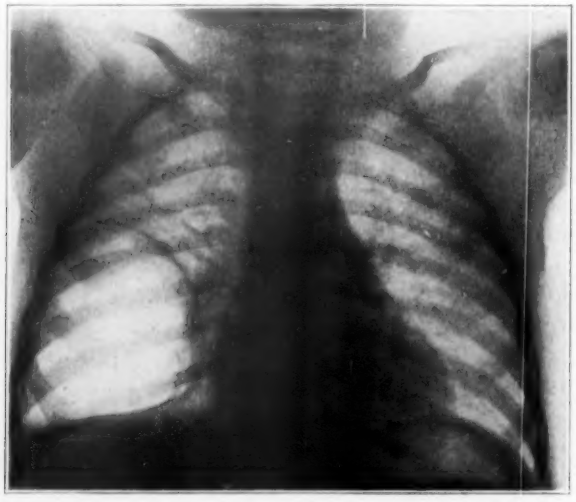

Fig. 8.—Localized pneumothorax following bronchopneumonia.

loss of lung markings. The periphery of these areas was a thick, sharp, smooth line (fig. 9). At no time was fluid or a fluid level present, and the patients did not have a productive cough.

Postmortem examination of several patients revealed marked subpleural bullae and blebs, as described by Miller.[2] These blebs and bullae were due to the rupture of an alveolus which allowed air to separate the visceral pleura from the parenchyma of the lung. They varied in size from that of a pinhead to that of a quarter, while some were narrow and extended for several centimeters. Diligent examination of the films of excised lung tissue and of the chest, both ante mortem and post mortem, failed to show any evidence of these lesions.

2. Miller, W. S.: Human Pleura Pulmonalis: Its Relation to Blebs and Bullae of Emphysema, Am. J. Roentgenol. **15**:399 (May) 1926.

They have been described as a possible cause of the annular shadows often found in films, but my observations do not bear this out.

PATHOLOGIC CHANGES IN THE MEDIASTINUM

The width of the mediastinal shadow may vary, especially in infants, in different exposures, depending on the phase of respiration, that is, the position of the diaphragm, which may give the impression of the shadow of the thymus gland (fig. 10). This deception can usually be detected by counting the ribs denoting the height of the diaphragm.

The shadow of the thymus, when seen, was usually bilateral with convex or straight borders, extending downward from the junction of

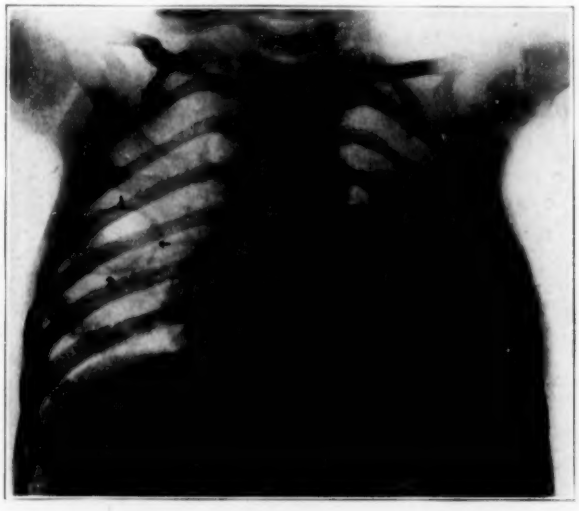

Fig. 9.—Right localized pneumothorax. Over the left side of the chest there is a shadow due to a thickened pleura and to empyema.

the clavicles with the sternum, and appearing to overlap the shadow of the heart. A large shadow did not always denote a heavy thymus, for, pathologically, some of the largest found were of the thick, narrow type not casting a wide shadow. Frequently when the position of the child was not straight, a unilateral convex shadow was seen extending out from the mediastinum, which resembled a unilateral thymic shadow. In a few patients observed roentgenographically for thymic enlargement, there was no thymic shadow or only a very small one, while on successive films taken shortly afterward, there was a large characteristic thymic shadow. No explanation for this was found. No shadow was seen with a concave border due to the thymus. There was one type of mediastinal shadow with concave borders that was seen frequently

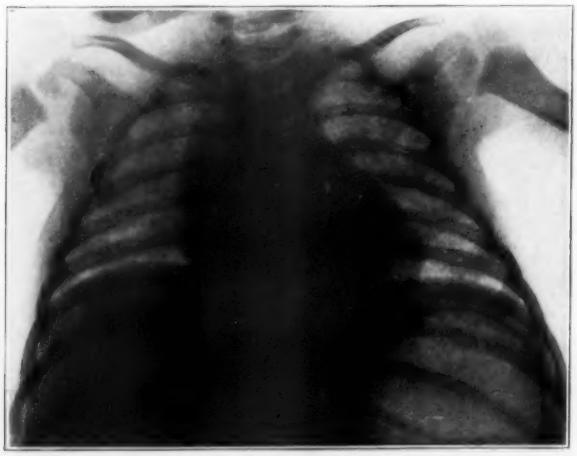

Fig. 10.—Widening of the mediastinal shadow due to a high diaphragm, the sixth interspace; no thymic enlargement; bilateral bronchopneumonia.

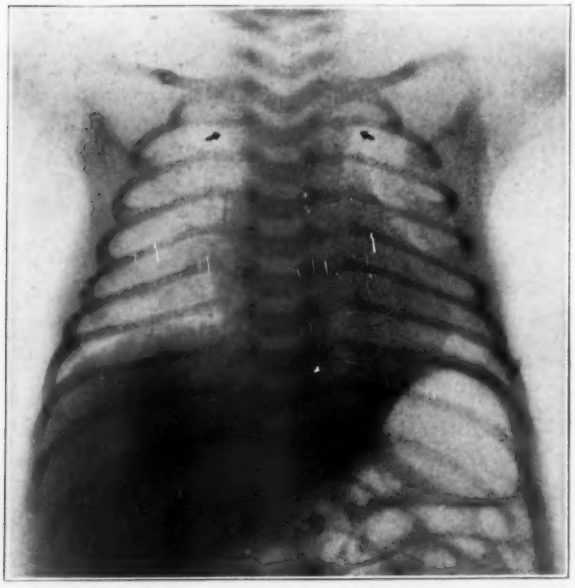

Fig. 11.—A wide mediastinal shadow with concave borders due to the great vessels of the neck; no thymic enlargement.

and that was described by McPhedran [3] in 1927. The shadow was usually bilateral. It began just above the heart in the region of the great vessels and flared out laterally until it reached the tissues of the neck near the inner ends of the clavicles. The borders of this shadow were regular and smooth, and curved inward (fig. 11). It was due to the subclavian vessels extending into the neck, which have a more lateral course in some children than in others. In some cases, the upper part was so wide as to give the apexes a clouded appearance.

In cervical and thoracic Pott's disease with the formation of a cold abscess there was often a characteristic shadow in the mediastinum or beneath the shadow of the heart. It was usually a large spindle-shaped shadow, or one with straight borders, its width depending on the size of the abscess (fig. 12). The borders were usually distinct and smooth.

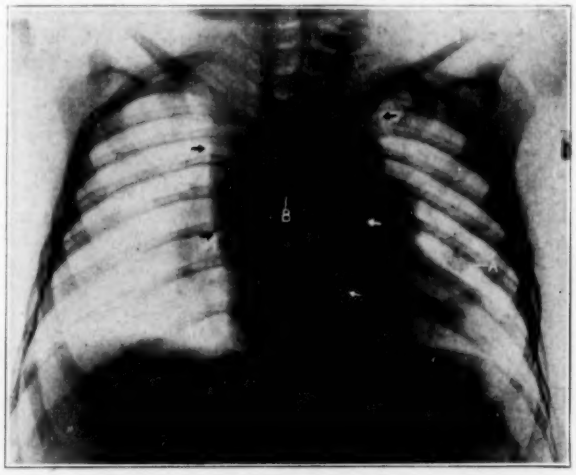

Fig. 12.—A wide mediastinal shadow due to a cold abscess and thoracic Pott's disease at (*B*) and a calcified primary focus (*A*).

When beneath the heart, its outline could usually be seen better with heavy penetration. Identification of the condition of the bone clinched the diagnosis.

The mediastinum is also a favorite location for the metastasis of malignant conditions. There were three cases of this sort with marked changes in the mediastinum, giving rather characteristic shadows. The enlargement of the medistinum was found to be of unequal proportions. Areas bulged into the pulmonary fields with smooth, regular convex borders. Only one such area might be present (fig. 13), but often several similar rounded areas were seen sometimes overlapping each other and presenting a scalloped appearance (fig. 14). In those cases,

3. McPhedran, F. M.: The X-Ray Diagnosis of Pulmonary Tuberculosis in Children, Am. Rev. Tuberc. **16**:420 (Oct.) 1927.

checked pathologically, the areas were due to large malignant lymph nodes that by their growth pushed their way into the chest cavity, encroaching on the pulmonary fields. Similar shadows might be present in Hodgkin's disease, lymphosarcoma and leukemia in which the involvement of the mediastinal lymph nodes is not metastatic but primary. Malignant metastatic involvement of the pulmonary tissue may be present with or without involvement of the mediastinum. At first, the shadows may simulate those of bronchopneumonia, but later they become large areas of increased density with irregular borders which may merge

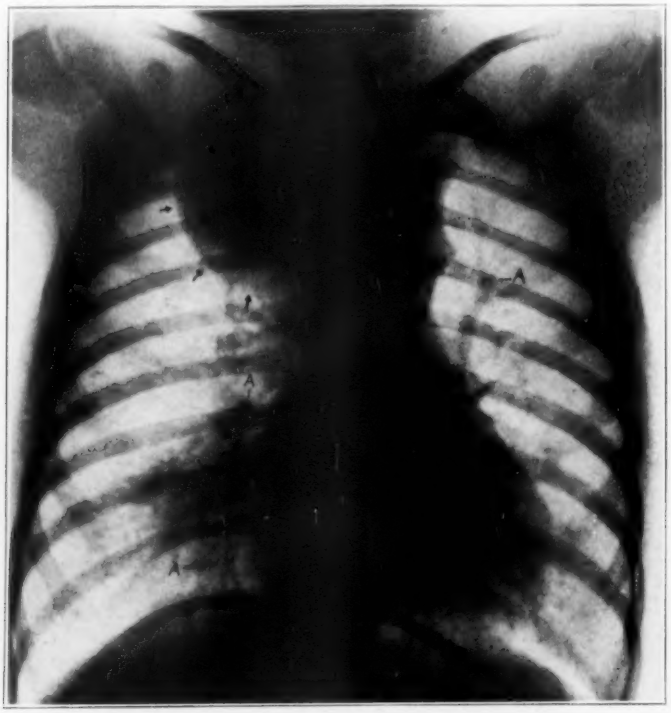

Fig. 13.—A bulging shadow due to a tumor in the mediastinum; bronchopneumonia of both lower lobes of the lung. *A* indicates the rounded shadows due to blood vessels.

into each other. The distribution is generalized and the individual shadows are much larger than those seen in miliary tuberculosis of the lungs, with which there should be no confusion.

SUMMARY AND CONCLUSIONS

The lungs of 171 children coming to necropsy were studied to determine what pathologic changes were present to account for the observations in roentgenograms of the chest.

The incidence and mortality of bronchopneumonia are higher than those of lobar pneumonia. Bronchopneumonia may be pseudolobar with shadows restricted to one lobe, but most frequently it has a wider distribution and is represented by areas of increased density with a patchy appearance.

A thickened pleura may be represented by a dense shadow along the lateral chest wall, or by various sized areas of increased density involving portions of the pulmonary fields through which lung mark-

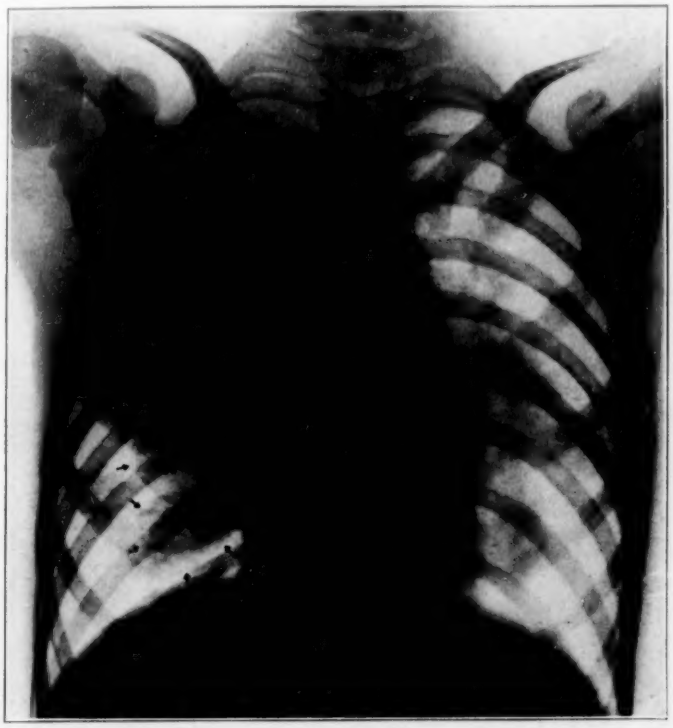

Fig. 14.—Great enlargement of the right mediastinal shadow owing to the metastasis of a malignant condition to the lymph nodes. Note the smooth, rounded borders of the shadows encroaching on the pulmonary fields.

ings can be seen. Pleural adhesions are found pathologically more frequently than on the roentgenograms.

In simple empyema, there is never a change in the fluid level with a change in the position of the patient. In an early stage, when fluid is accumulating in the pleural cavity, a definite shadow can be seen demarcating it from the lung which it floats.

Pneumothorax and pyopneumothorax are not rare in children, and their presence does not mean a fatal termination. In all cases coming to necropsy, a connection with a bronchus was found. They occur frequently from pleural puncture, both diagnostic and therapeutic.

The shadow of a thymus has a convex or straight border in contrast with a broad mediastinal shadow with concave borders, due to the great vessels of the neck.

Metastatic malignant involvement of the mediastinal lymph nodes is not rare, and casts a characteristic type of bulging shadow with smooth borders.

707 Fullerton Avenue.

BLOOD DIPHTHERIA ANTITOXIN STUDIES*

RANDOLPH G. FLOOD, M.D.
SAN FRANCISCO

For the past few years, I have been somewhat dubious of the true value of the Schick test. This doubt was crystalized during the epidemic of diphtheria in 1923, when several children and nurses who had responded with negative reactions to carefully controlled Schick tests developed the disease.

This was the impetus which started me actually to titrate the blood diphtheria antitoxin in subjects who were known to have either positive or negative Schick reactions and, later, to extend the work to measure the blood antitoxin response of various groups following injections of diphtheria toxin-antitoxin.

TECHNIC

In order to accomplish this work, it was necessary to have a technic that was accurate, simple and economical. Two methods were open: that of Zingher,[1] which was found to be incorrect in its dilutions, and that of Roemer.[2] The latter method was practical, but the end-points were not sharp enough to make close differentiations between the small amounts of antitoxin found in the bloodstream.

The method that was finally developed was based on my observation that 1/450 minimum lethal dose of diphtheria toxin causes a definite erythema but no slough when injected intradermally into the skin of a guinea-pig.

With this fact in mind, the dilutions shown in table 1 were so arranged that if the tested serum contained the expected amount of antitoxin, a surplus of 1/450 minimum lethal dose remained in the amount injected into the animal. This caused a distinct erythema but no necrosis.

If the serum contained less than the expected amount of antitoxin a slough resulted, as more toxin was left unbound. However, if the serum contained more that the expected amount, a residue of less than 1/450 minimum lethal dose resulted and no reaction occurred.

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* Submitted for publication, Aug. 5, 1929.

* Read before the Section on Diseases of Children at the Eightieth Annual Session of the American Medical Association, Portland, Ore., July 10, 1929.

1. Zingher, A.: Proc. New York Path. Soc. **17**:28, 1971.

2. Roemer, P. H.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **3**:343, 1909.

The technic is simple, and experience has shown that the best results are obtained by the following procedure:

After the dilutions are mixed, they are placed in the icebox for seven hours, and the tubes are shaken frequently. At the end of this time, the injections are made with a tuberculin syringe through a drop of collodion placed on the skin to prevent leakage. Four tests are made in the skin of the belly of a white guinea-pig, and the reaction is read at

TABLE 1.—*Dilutions Used in Tests*

Standard Toxin, Cc. (1 Cc. = 1/45 L + Dose	Saline, Cc.	Serum, Cc.	Antitoxin in 1 Cc. of Serum if Erythema Results, Units	Amount Injected, Cc.
0.2	0.0	0.4	1/90	0.3
0.2	0.1	0.3	1/60	0.3
0.2	0.0	0.2	1/45	0.2
0.4	0.2	0.2	1/22	0.2
1.0	0.8	0.2	1/9	0.2
2.0	1.8	0.2	1/4	0.2
4.0	3.8	0.2	1/2	0.2
8.0	7.8	0.2	1	0.2
16.0	15.8	0.2	2	0.2
32.0	31.8	0.2	4	0.2

TABLE 2.—*Results in Titration of the Blood Antitoxin of Children Giving Positive and Negative Reactions to the Schick Test*

Positive Schick Reaction*			Negative Schick Reaction†		
Name	Age, Year	Units of Antitoxin per Cc. of Blood	Name	Age, Year	Units of Antitoxin per Cc. of Blood
Louis A. B.	4	0.0	Patricia S.	9	1/30
Margaret K.	7	0.0	Bernice B.	6	1/90+
Paul K.	6	1/90	Veronica B.	7	1/60
Norbet P.	10	1/60	Mary K.	4	0.0
Louise P.	10	1/45	James V.	10	1/30+
Joe K.	7	0.0	James S.	5	1/90+
Ernst C.	6	0.0	Peter R.	7	1/30
James T.	5	0.0	Joe V.	11	1/30
Robert K. R.	4	1/90+	Beatrice D.	7	1/30
Mary K. R.	6	0.0	Jerome F.	5	1/90+
Bernard D.	3	0.0	Robert F.	6	1/45
Cecil D.	6	1/60	Kelly Mc.	4	1/90
Terence H.	4	1/90	Betty D.	6	1/30
Patrick H.	7	1/90+	Lucile H.	5	1/45
David R.	9	1/60	Kathleen O'D.	4	1/60

* The percentage of error was 6.6, on the assumption that a positive Schick reaction means less than 1/50 unit of antitoxin per cubic centimeter of blood.

† The percentage of error was 46.6, on the assumption that a negative Schick reaction means more than 1/50 unit of antitoxin per cubic centimeter of blood.

the end of forty-eight and seventy-two hours. The end-point will be sharp.

This method is accurate to 5 per cent, as shown by the use of checks of standard antitoxin.

Having developed an accurate method, I next titrated the blood antitoxin of children giving positive and negative reactions to the Schick test, and tabulated them as shown in table 2. It has been assumed that a negative reaction to the Schick test indicates that that person has at

least 1/50 unit of antitoxin per cubic centimeter in his blood. However, as can be seen from the chart, 46 per cent of the children with negative reactions did not have a blood titer up to expectancy. On the other hand, there was a discrepancy of only 6.6 per cent of actual titer and reaction in children who gave positive reactions to the Schick test. In short, a positive reaction to the Schick test has real significance, while I believe a negative reaction is usually misleading and should not be accepted as the final criterion for immunity to diphtheria.

The next step was to measure the diphtheria antitoxin content of the blood in groups of children at stated intervals following the injection of toxin-antitoxin, and in this way to learn the response in terms of blood antitoxin.

The first group observed were children who had a positive Schick reaction and an actual blood antitoxin titer below 1/30 units per cubic

Fig. 1.—Reaction from a test injection into a guinea-pig. The serum used contained 1/45 unit of antitoxin per hundred cubic centimeters. Dilutions were made according to table 1. The third dilution represented by third injection in upper left-hand quadrant, gives a distinct erythema, but no slough as in the fourth. This is the sharp end-point in this determination.

centimeter. The results of repeated tests are shown in figure 2. It will be observed that most of the children acquired 1/30 unit of antitoxin per cubic centimeter of blood between the third and fourth month. The response of the individual child could not be foretold, but as a rule those who had a small amount of natural antitoxin acquired a final titer somewhat higher than those who started from 0 units.

The next group tested consisted of children who had a negative Schick reaction and an actual blood antitoxin titer of 1/30 units or over, I was particularly interested in this group as it had been stated that a child with this amount of antitoxin in his blood would not be stimulated by the toxin-antitoxin, because the free toxin which has most of the

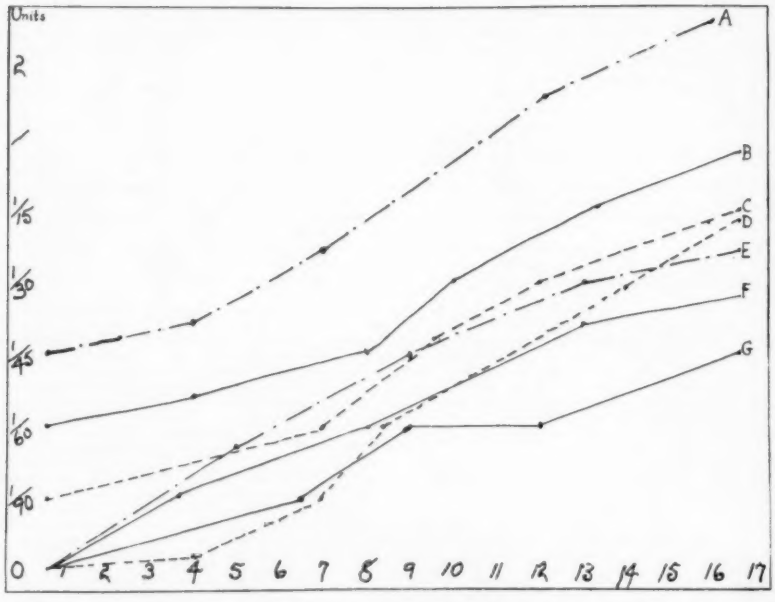

Fig. 2.—The effect of the injection of diphtheria toxin-antitoxin on the antitoxin content of the blood of children giving a positive Schick reaction. The letters at the right indicate the subjects tested: *A*, Louise P. (10 years); *B*, Norbet P. (10 yeras); *C*, Paul K. (6 years); *D*, Joe K. (7 years); *E*, Ernst C. (6 years); *F*, Margaret K. (7 years), and *G*, James T. (5 years). In this and subsequent charts, the vertical scale at the left indicates the number of units of antitoxin per hundred cubic centimeters of blood, and the figures along the bottom of the chart, the period of observation by weeks.

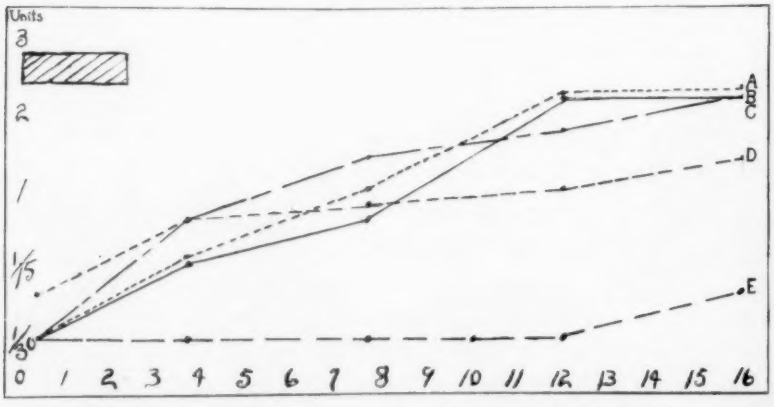

Fig. 3.—The effect of the injection of diphtheria toxin-antitoxin on the antitoxin content of the blood of children giving a negative Schick reaction. The subjects tested were: *A*, Patricia S. (9 years); *B*, James V. (10 years); *C*, Peter R. (7 years); *D*, Joe V. (11 years), and *E*, Beatrice D. (7 years). The small rectangle in the upper left-hand corner of this and the subsequent two charts indicates the period of time during which the injections of toxin-antitoxin were administered.

antigenic properties would be neutralized. However, this was not the case, as can be seen in figure 3, as these children responded even more readily that those in the former group, with one exception (B. D.); this case will be described later.

The response of these children emphasizes one point: that it is not the free toxin which acts as the antigen but the altered toxin or toxoid. This is also borne out by the immunizing results of the anatoxin of the French, which contains no free toxin.

This group of children differed from the former in that they showed almost an immediate response of increased blood antitoxin.

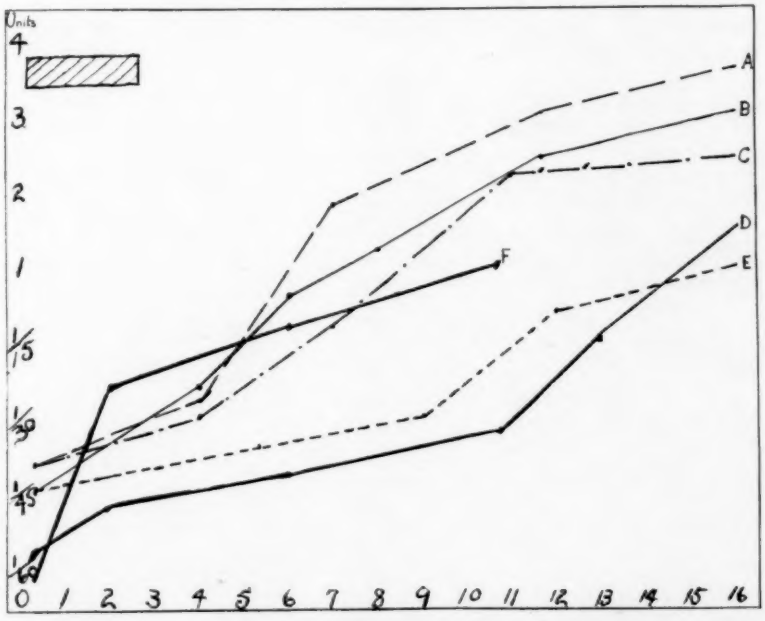

Fig. 4.—The effect of the injection of diphtheria toxin-antitoxin on the antitoxin content of the blood of adults (nurses) giving a positive reaction to the Schick test. The subjects were: *A*, Mrs. Shee.; *B*, Miss E. P.; *C*, Miss Mant.; *D*, Miss Cl.; *E*, Miss Cav., and *F*, Miss D.

Their final titer, however, was about the same as that of the group giving a positive Schick reaction.

For the third group nurses were selected, as I was anxious to observe whether young adults who gave a positive Schick reaction would respond differently than a group of children giving positive Schick reactions.

It will be observed from figure 4 that all these subjects possessed some natural antitoxin. Their response to the injections of toxin-

antitoxin was much more rapid and irregular, with a final higher titer than that of the children.

The explanation is evident: When one acquires diphtheria immunity one acquires two things: (1) a sufficient amount of antitoxin in the blood stream to give protection against immediate infection, and (2) the ability to respond rapidly with a mobilization of antibodies following stimulation by the antigenic substance. Many persons lose their antibodies in the blood stream after they become immune, but they always retain the ability to produce new antibodies rapidly when stimulated.

It is interesting in this connection that in the commercial production of diphtheria antitoxin, old horses, which have some natural immunity, are selected, as they respond more rapidly and have a higher final titer than young animals.

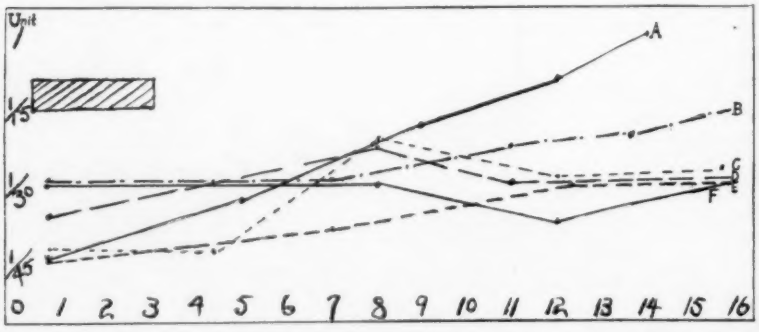

Fig. 5.—The effect of the injection of diphtheria toxin-antitoxin on the antitoxin content of the blood of true carriers. The subjects were: *A*, Walter B. (8 years); *B*, Miss Can. (nurse); *C*, John K. (7 years); *D*, Miss Hat. (nurse); *E*, Weiler H. (5 years), and *F*, Betty D. (6 years).

Evidently some of the nurses tested had lost some of their antitoxin titer, but still retained their ability to respond readily to stimulation. Others responded exactly as did the children in the group giving a positive Schick reaction. The explanation lies in their past history: The majority who responded like children came from a rural environment, while the others were of urban origin.

In the final group, which was limited in number, the endeavor was made to measure the antitoxin response of true carriers, that is persons who harbored virulent diphtheria bacilli without clinical symptoms. This group had sufficient antitoxin to give a negative Schick reaction, as shown in figure 5.

It will be noticed that this group was particularly resistant to the stimulating effect of toxin-antitoxin. It was extremely difficult to raise their blood antitoxin titer, and the height to which it could be raised was limited.

The significance of this is obvious. I feel that the carrier has a fundamental inability to respond to antigenic stimulation, and that it might be possible to determine potential carriers if one could titer all toxin-antitoxin recipients for their blood response.

It is interesting to note here that Beatrice D. (fig. 2) responded almost identically as did her younger sister Betty who was a true carrier.

This brings up the question of individual response to an antigenic stimulant and whether it may be familial. It is my belief that more work is required along these lines before this question can be answered satisfactorily. However, I feel that in measuring the exact antitoxin response to a known and measured antigen, such as toxin-antitoxin, marked individual variations will be found among the subjects tested.

SUMMARY

1. A simple, economical and accurate method of determining small amounts of blood antitoxin has been described.

2. The blood of a group of children with positive and negative Schick reactions was titrated for antitoxin, with the result that 46.6 per cent of the children giving a negative Schick reaction did not have 1/50 unit of antitoxin.

3. In a group of children giving a positive Schick reaction, repeated titrations were done; the subjects were found to acquire 1/30 units of blood antitoxin between the third and fourth month.

4. In a group of children giving a negative Schick reaction, similar titrations were done on all who possessed at least 1/30 unit of antitoxin; they were found to respond even more readily that the preceding group, a fact which suggests that the antigen value is in the toxoid and not in the free toxin of the toxin-antitoxin mixture.

5. Young adults respond more rapidly than children and acquire a higher titer.

6. Children who have been true carriers are resistant to injections and build up their antitoxin extremely slowly.

490 Post Street.

ABSTRACT OF DISCUSSION

DR. W. H. KELLOGG, San Francisco: Dr. Flood has brought out some rather important points. One is the development of antitoxin in the blood following immunization, and that this requires a definite interval of time and varies in different persons. He referred also to persons whose antitoxic titer seems to differ somewhat from the indications given by the Schick test. I think it is a settled point that there is such a thing as a latent immunity; the cellular immunity referred to by Dr. Schick is an example, and it has been noted in some parallel tests with the Schick and the Kellogg tests that I have already reported. These tests showed that a few persons who were immunized with toxin-antitoxin gave a positive result by the guinea-pig method, and

yet gave a negative Schick reaction—which is apparently a contradiction. I think this is answered by the suggestion of Schick that there is a cellular immunity, that these persons have the capacity to rise to the occasion when exposed to infection, and that they rapidly develop an antitoxic immunity. As I developed this Kellogg test referred to by Dr. Flood, I shall answer the suggestion that has been made that I would detract from the value of the Schick test because of having given out this laboratory method of testing. This is not the case. The Schick test, when properly performed with a toxin of known potency, is an accurate test, one of the most accurate, I think, of the skin tests used for various purposes. But not everyone can use the Schick test safely and satisfactorily. One of the chief sources of trouble in using the Schick test to determine susceptibility and immunity to diphtheria is the instability of the diphtheria toxin that is used in applying this test; light, heat and exposure to air cause a deterioration and a conversion of toxin into toxoid, and a false negative may be secured, against which one has no control.

Therefore, a practicing physician who is testing only a few children should never attempt to use the Schick test, not because he might not be able to read it properly, but—leaving aside all such questions as pseudoreaction—because deterioration of toxin is such a common occurrence that a laboratory test is the most dependable if one has only a few tests to make. For large numbers of children, the skin test is another matter; there are occasions when it is the most practical and the easiest test to apply. The guinea-pig test, however, is the most accurate. It is an absolute titration and is immune to those disadvantages to which I have referred.

Dr. Randolph G. Flood, San Francisco: I am a great believer in Dr. Kellogg's test. I feel that it should displace the routine Schick test in most of the pediatric practice. I purposely avoided saying anything about cellular immunity. It will be observed from the title of the paper that I dealt exclusively with blood antitoxin. However, as time goes on and work like this develops, I find that in order to answer questions properly I have to be sidetracked to a related problem: How soon does the skin reaction, or the Schick reaction, turn negative as the antitoxin is increased in the bloodstream? I am trying to approach that today by taking a series of young nurses who give a positive Schick reaction—in other words, subjects who have no antitoxin according to the Schick test, and who show no antitoxin on titer—and by giving them toxin-antitoxin injections; I then subject them to repeated Schick tests and note when the skin begins to assume its immunity against the diphtheria toxin. I did not care to discuss this subject, but so far two or three of these nurses have been followed for about three months. I would say that the antitoxin titer in the blood increases before the Schick reaction becomes negative. One nurse has a titer today of $\frac{1}{15}$ unit of antitoxin, and still gives a positive reaction to the Schick test.

FAMILIAL HEMOLYTIC ANEMIA OF CHILDHOOD—VON JAKSCH *

MARTHA WOLLSTEIN, M.D.
AND
KATHERINE V. KREIDEL, A.B.
NEW YORK

Five of the ten patients on whom splenectomy has been performed at the Babies' Hospital show a sufficient number of points in common to warrant grouping them as examples of a familial, hemolytic type of infantile anemia which is not cured by splenectomy. The postoperative reaction is a form of marrow stimulation expressed in large numbers of normoblasts in the circulating blood. Four of the five children died. The brother of one of the patients and three others with a similar blood picture, three of whom were not operated on, have been added to the group. Thus are included two brothers in whose family three other cases were said to have occurred, a brother and sister, a boy whose family history shows one similar case and four girls without a familial history. Six of the families were Italian, and one was Greek. All of the nine children were born in or near New York City.

REPORT OF CASES

CASE 1.—F. P., a white boy, aged 3 years, was admitted to the hospital with a history of anemia of two and a half years' duration. Both parents were well. Four children were dead. The parents said that one child died of anemia at the age of 4 months, another at 14 months, and a boy who had been in the Babies' Hospital with the diagnosis of von Jaksch's anemia (case 2) died when 9 months old. A fourth child died of anemia when 3½ years old. The pallor of the patient was noticed at the age of 5 months, and he became progressively worse, in spite of excellent care with plenty of fresh air and sunshine. He never had any acute, contagious disease.

On admission, he was poorly nourished and anemic. There was no jaundice and no history of hemorrhage. The liver was palpable a little below the costal margin. The spleen was greatly enlarged, the lower border extending below the umbilicus to a point 8 cm. below the costal margin. The blood showed 38 per cent hemoglobin, 1,500,000 red cells and 9,000 leukocytes. There were 39 per cent polymorphonuclears and 3 per cent myeloblasts. From two to three nucleated red cells per hundred leukocytes were found. A blood transfusion of 180 cc. failed to bring about improvement in the blood count, and the hemoglobin rose to only 52 per cent. Splenectomy was performed by Dr. Downes. The spleen measured 14 by 10 cm. Its capsule was smooth and not thickened. The cut surface showed the malpighian bodies distinctly, and the pulp was quite firm. On microscopic

* Submitted for publication, July 18, 1929.

* From the Babies' Hospital and the Pediatric Department of Columbia University College of Physicians and Surgeons.

examination the connective tissue was normal, the malpighian bodies closely packed with lymphocytes, and the germ centers few and small. The sinuses were large, and contained numerous mononuclear eosinophilic cells as well as polymorphonuclear leukocytes and red cells. The outstanding lesion was congestion and dilatation of the pulp spaces, with the presence of the eosinophil cells.

The child recovered from the operation, and his general condition improved. His blood showed 50 per cent hemoglobin, 2,000,000 red blood cells, 7,000 white cells and 148 nucleated red cells per hundred leukocytes. Two months after operation it was found necessary to give a transfusion, because he had lost ground and the hemoglobin was 35 per cent. He acquired a dysentery infection from which he recovered, but died five months after operation without ever having been well. No autopsy was obtained.

Case 2.—V. P., the brother of F. P., had been a patient in the hospital eight years previously, having been admitted at the age of 7 months with a diagnosis of von Jaksch's anemia for which he was given a blood transfusion. The anemia apparently dated from "an attack of fever" at the age of 6 months. On admission the spleen was felt 6 cm. below the costal margin, and the liver 5 cm. below. The superficial lymph nodes were generally enlarged. All were discrete, and the largest was 1 cm. in diameter. The hemoglobin was 30 per cent, the red blood cells less than 2,000,000, and the white blood cells 35,000. There were 7 normoblasts to 100 leukocytes.

After direct transfusion of 200 cc. of the father's blood the hemoglobin rose to 65 per cent, and the red blood cells to 5,000,000 with 15 normoblasts to 100 leukocytes. One week later he was discharged in good condition, but after the lapse of one month he returned in a more anemic state, and died at home a few weeks later. When he was last seen, the spleen had extended 10 cm. below the costal margin.

Case 3.—S. G., a boy, aged 4 years, was admitted for pallor and weakness, said to have been present since birth. A brother died at 11 months "of the same trouble"; otherwise the family history was unimportant. The patient had pertussis followed by measles at 3 years of age. About three months before admission swelling of the face, abdomen and extremities appeared. The child was tired and sleepy; his skin was lemon yellow, but he was not jaundiced. The spleen extended below the umbilicus, almost to the crest of the ileum. The blood showed 35 per cent hemoglobin, 3,500,000 red cells of normal fragility and 19,600 leukocytes. There were 16 nucleated red cells to 100 leukocytes.

In spite of three transfusions with the mother's blood, the boy failed to improve, and splenectomy was done by Dr. Downes four months after admission to the hospital. He recovered from the operation and was discharged in good condition five weeks later. The striking feature of the blood was the postoperative increase of nucleated red cells from 35 seven days after splenectomy to 202 at the time of discharge, 442 after eight months, 1,455 after three and two-thirds years and 701 three weeks before his death, four years after the removal of the spleen. Although the boy had been able to get about and go to school, he had never been normal. His color remained sallow, his features broadened and flattened[1] (fig. 1), and his bones showed a general rarefying process apparent in all the extremities (fig. 2). The feces contained an increased amount of urobilinogen.

Case 4.—B. S., a girl, aged 25 months, was brought to the Babies' Hospital on April 4, 1924, because she had been losing weight and appetite for four months,

1. Cooley, T. B.: Von Jaksch's Anemia, Am. J. Dis. Child. **33**:795 (May) 1927.

during which time she had been becoming more and more pale. Her weight at birth was said to have been 12 pounds (5,443 Gm.). She was nursed for seven months, and then fed on orange juice and a milk formula with the gradual addition of vegetables, cereals and soups. Her parents were both born in Greece. Two children were living and two were dead. One died of pneumonia and measles. Another, a boy, died when 4½ years old one year after his spleen had been removed at the Nursery and Child's Hospital.[2] B. S. was poorly nourished and developed, pale and apparently chronically ill. The axillary, cervical and inguinal lymph nodes were moderately enlarged. The spleen extended 7 cm. below the ribs in the mammary line. The liver extended 4 cm. below the costal border. The Pirquet skin test was negative. The urine was normal. The blood showed 2,704,000 red cells, 43 per cent hemoglobin, 18,069 leukocytes with 63 polymorphonuclears, 21 lymphocytes and 15 monocytes. The platelets numbered 116,000. There were 43 nucleated red cells per hundred leukocytes. Poly-

Fig. 1 (case 3).—Picture taken three weeks before the boy died, showing widening of the malar bones and flattening of the features.

chromasia, achromasia anisocytosis (microcytes and macrocytes) and poikilocytosis were all present. The Wassermann reaction was negative.

After removal of the tonsils and adenoids, the hemoglobin fell to 22 and the red cells to 1,404,000, while the platelets numbered 72,000. After transfusion of 140 cc. of the father's blood, the platelets rose to 96,000, the hemoglobin to 40 per cent and the red cells to 2,312,000. The child did well at home for a month, returned in about the same condition and developed double otitis media which required incision of both ear drums. At that time the platelets had risen to 184,000; the red cells had fallen below 2,000,000 and the differential count remained the same. Some stippled red cells were seen.

Splenectomy was decided on, and after a second transfusion of 150 cc. it was performed on Aug. 27, 1924, by Dr. Bolling. The child made an uneventful

2. Denzer, B. S.: A Critique of Von Jaksch Anemia, Arch. Pediat. **44**:537, 1927.

recovery from the operation, and also from an attack of bronchopneumonia in November, 1924. The platelets gradually increased, but the hemoglobin ranged from 20 to 40 per cent, and the red cells around 2,500,000. The most interesting and striking thing about the blood was the large number of nucleated red blood cells constantly present after operation, as many as 1,500 per hundred leukocytes (fig. 3). Three and two-thirds years after splenectomy, when the child was 6 years old, she

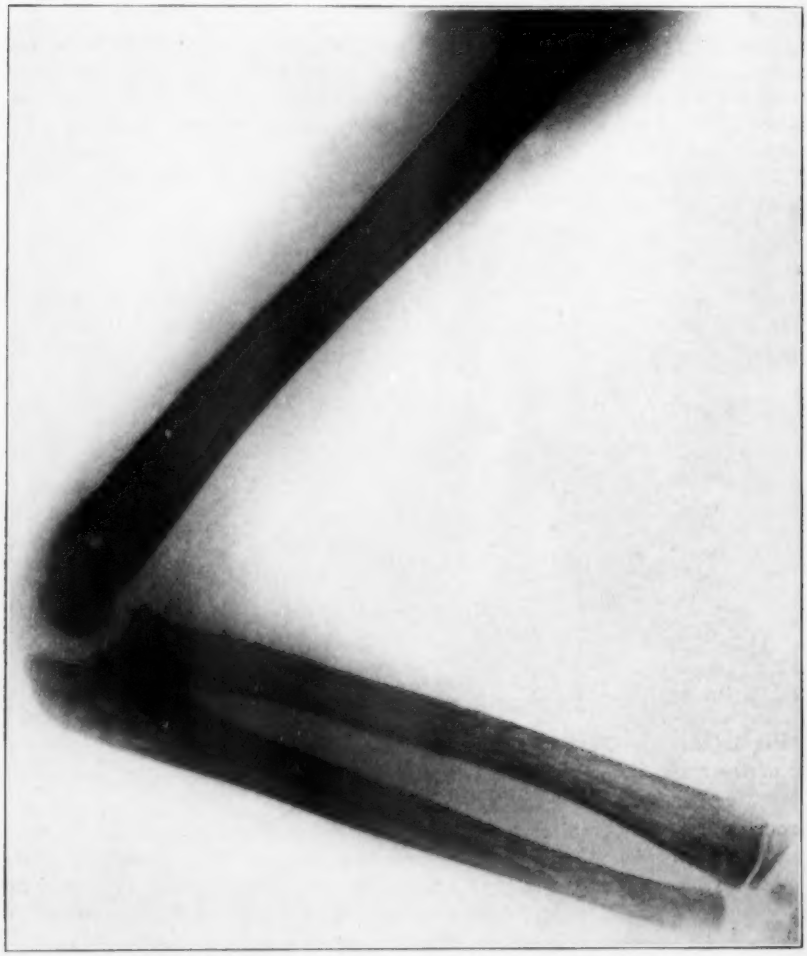

Fig. 2 (case 3).—Humerus, radius and ulna showing rarefaction of the shafts.

came back to the hospital with an acute bronchitis from which she recovered, but as the hemoglobin had fallen to 15 per cent she was given a transfusion of 300 cc. of the father's blood. Thereafter, the hemoglobin rose to 35 and the red cells to 2,704,000. Before transfusion the icteric index had been 25, the indirect van den Bergh reaction positive, and the urine contained urobilinogen in a dilution of 1 to 40. A series of blood counts are given in table 1, and figure 4 shows the fluctuation of the nucleated red cells before and after operation. Roentgeno-

grams of the bones showed rarefaction in all the long shafts (fig. 5), a slight degree of widening of the malar bones and flattening of the features, as described by Cooley.[1]

During the following three months the child did not improve, but remained pale, tired easily, and in July, 1928, developed attacks of fever (104 F.) every third day. Quartan parasites were found, and 4 grains (0.26 Gm.) of cocoaquinine was given daily. The paroxysms ceased two days after treatment was begun, and no more plasmodia were found. After a transfusion of 100 cc., she was sent home in fair condition, and when seen on Sept. 28, 1928, she seemed bright and happy and attended school regularly. The parents denied any malarial infection. They

TABLE 1.—*Blood Counts in Case 4, Over a Period of Five Years*

Date	Red Blood Cells	Hemoglobin	Platelets	White Blood Cells	Polymorphonuclears	Lymphocytes	Mononuclears	Eosinophils	Normoblasts	
4/ 5/24	2,512,000	40	.....	10,032	47	43	10	..	24 (3,200 per c.mm.)	Achromasia, anisocytosis, poikilocytosis
4/ 9/24	2,704,000	43	116,000	18,069	63	21	15	1	43 (13,630 per c.mm.)	
5/17/24	Tonsillectomy									
5/19/24	1,404,000	22	72,000	12,400	70	24	11	..	11	
	Transfusion, 140 cc.									
7/10/24	1,060,000	35	144,000	11,862	37	54	5	..	21 (3,178 per c.mm.)	Myelocytes, 4
8/25/24	Transfusion, 150 cc.									
8/27/24	Splenectomy									
9/ 5/24	2,432,000	40	192,000	24,500	65	3	20	..	90 (22,200 per c.mm.)	Myelocytes, 4; myeloblasts, 8
9/23/24	2,224,000	40	264,000	14,000	27	46	19	1	290 (42,400 per c.mm.)	Myelocytes, 4; myeloblasts, 3
10/1/24	2,592,000	45	184,000	20,300	40	11	39	7	767 (145,700 per c.mm.)	Myelocytes, 2; myeloblasts, 1
6/ 7/25	2,304,000	40	424,000	18,850	57	40	17	3	857 (151,550 per c.mm.)	Myelocytes, 2; myeloblasts, 1
1/ 9/27	1,432,000	25	304,000	10,420	35	51	11	2	1,575 (163,980 per c.mm.)	
4/12/28	1,608,000	25	456,000	11,100	65	32	1	1	957 (95,300 per c.mm.)	
4/22/28	Transfusion									
4/23/28	2,704,000	35	488,000	14,000	51	42	6	..	566 (83,300 per c.mm.)	Myelocytes, 1
6/28/28	1,528,000	20	384,000	18,500	53	45	2	..	321 (40,900 per c.mm.)	Myelocytes, 1; malarial plasmodia seen (quartan)
7/30/28	1,528,000	20	496,000	13,880	60	31	1	6	351 (39,940 per c.mm.)	No malaria plasmodia seen
3/13/29	1,704,000	30	528,000	5,300	47	48	2	2	2,016 (115,000 per c.mm.)	Megaloblasts, 5; myelocytes, 1

were born and bred in Sparta, a part of Greece not infected with malaria, and no recent arrivals from Greece had been in contact with the child. The malarial infection was apparently acquired at her home in Westchester. Repeated search of sections of the spleen failed to discover any plasmodia. It seems most improbable that malaria had previously been present, much less that it was the cause of this child's splenomegaly and anemia or of that of the younger boy in case 5.

On March 13, 1929, she was seen again, and the condition of the blood was distinctly worse (fig. 6). The nucleated red cells numbered 115,000 per cubic millimeter and about 0.25 per cent were megaloblasts, with a blue staining cytoplasm devoid of hemoglobin. Karyokinetic figures were numerous in the nuclei of both megaloblasts and normoblasts. The red cells varied in size and contained more than one unstained area. There were practically no normal red cells (fig. 6). Yet the child was happy, more talkative than her wont, and attended school regularly.

On Nov. 11, 1929, there were 2,424,000 red cells with 28 per cent hemoglobin and 13,500 white cells. Of these 49 per polymorphonuclears, 44 lymphocytes, 2 monocytes and 5 eosinophils. Seven hundred and forty-eight normoblasts (100,900 per cubic millimeter) were present to 100 leukocytes.

CASE 5.—N. S., a younger brother of B. S., was brought to the hospital at 11½ months of age because he was pale, could not stand, and his abdomen was increasing in size. There was moderate edema of the hands and feet. On admission the hemoglobin was 30, leukocytes 50,190 and red cells 1,824,000 with 324,000 platelets. There were 30 nucleated red cells to 100 leukocytes. The spleen

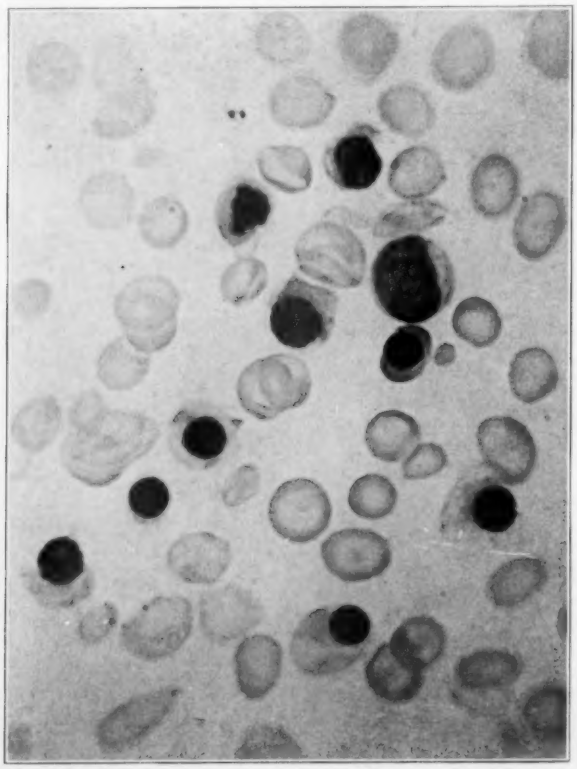

Fig. 3 (case 4).—Blood picture one year after splenectomy.

extended 7 cm. below the costal margin and the liver 5 cm. below. The inguinal and cervical nodes had a shotty feeling. After direct transfusion with 150 cc. of the father's blood, the hemoglobin rose to 65 and the red cells to 3,120,000. The leukocytes numbered 17,790, with 41 per cent polymorphonuclears. There were 33 nucleated red cells to 100 leukocytes. Many of the red cells showed stippling. Careful search failed to show malarial plasmodia. The Wassermann reaction was negative. A fragility test showed that the red cells were normal in their resistance to hemolysis.

The percentage of hemoglobin became gradually lower, and the red cells diminished in number. The nucleated red cells increased to 55 per hundred leukocytes. Stippling remained, and an increased number of reticulated red cells were

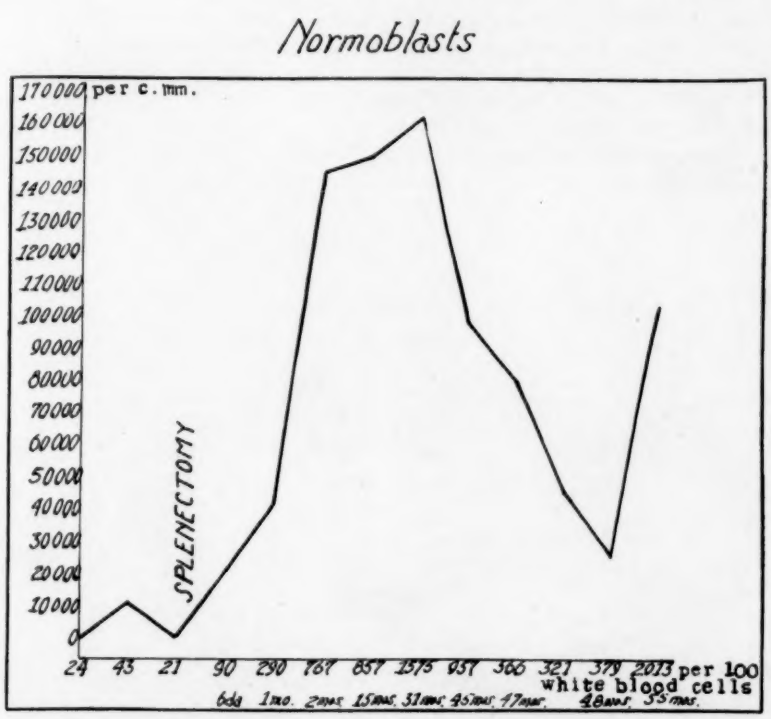

Fig. 4 (case 4).—Curve of the nucleated red cells over a period of five years; before and after splenectomy.

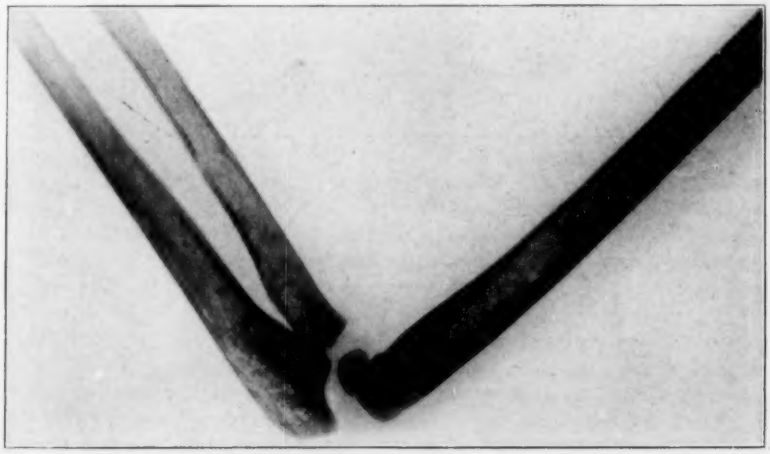

Fig. 5 (case 4).—Humerus, radius and ulna showing rarefaction of the shafts.

present. Edema of the hands and feet developed, and fluid was present in the abdomen as well. The urine showed only a trace of albumin and no casts. After a second transfusion the edema gradually disappeared, and the child seemed brighter. The blood showed practically no change, the hemoglobin having gone down to 35 per cent. On July 24, 1924, splenectomy was performed by Dr. Bolling. The spleen weighed 222 Gm. Two supernumerary spleens were left in place. Five days after operation the red cells numbered 2,500,000 per cubic millimeter;

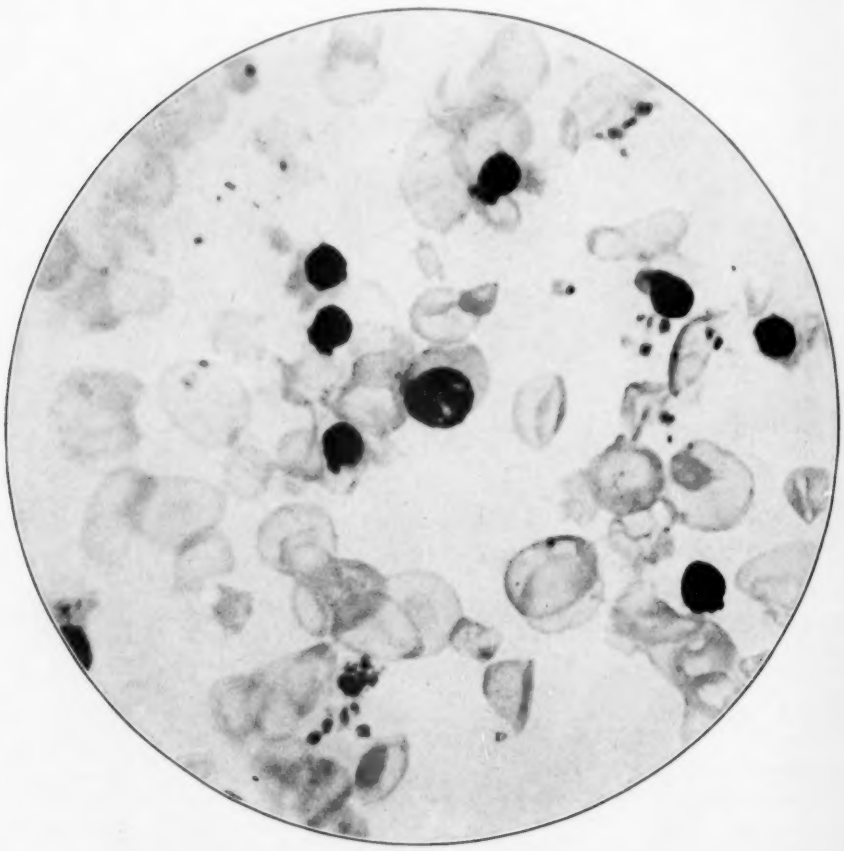

Fig. 6 (case 4).—Blood four and five-twelfths years after splenectomy, showing a megaloblast, normoblasts, Howell-Jolly bodies, poorly staining and friable red cells.

hemoglobin 40 per cent and leukocytes 9,700. All forms of nucleated blood cells were seen, numbering 637 to 100 white cells. There were 192,000 platelets. The main characteristic of the blood after the operation was the enormous number of nucleated red cells including macroblasts, microblasts and normoblasts. One month after operation the nucleated red blood cells numbered 198,000 per cubic millimeter. The hemoglobin stayed around 38 per cent and the leukocytes 20,000. The child's general condition remained about the same, though he had recovered from the operation and was playful. Four months afterward he developed an

infection of the upper respiratory tract, and died of bronchopneumonia in four days. At autopsy acute bronchopneumonia was found to occupy the right apex. The rest of the lungs were congested and edematous. There was a marked general bronchitis, tracheitis and laryngitis. The tracheobronchial and mesenteric lymph nodes were enlarged. In the splenic bed lay two supernumerary spleens, the smaller of which was bright red, 1 by 1 by 1 cm. in diameter. The larger weighed 6 Gm. and measured 3.5 cm. in diameter. On section it showed the friability of an acute splenic tumor. The suprarenal glands weighed 10 Gm. They were larger than normal, and on section the soft, red center contained fluid blood. The kidneys were united to form a horseshoe lying across the vertebral column. The kidney substance was congested. From the heart's blood and from the spleen, a pure growth of pneumococcus group IV was obtained. Microscopically, the supernumerary spleen showed widely dilated pulp spaces filled with red cells, lymphocytes, eosinophils and some pigment. Small hemorrhages were present. The liver showed a moderate number of cells which contained fat droplets. The interlobular connective tissue was cellular, and the interlobular angles showed collections of eosinophilic myelocytes, polymorphonuclear leukocytes and a few nucleated red cells. The intralobular capillaries were wide and contained many red cells and fewer leukocytes. The Kupffer cells contained some iron pigment.

CASE 6.—C. M., a white girl, aged 3 years, was admitted to the hospital because she had had fever and pallor for one month with epistaxis two weeks before. The family and developmental histories were without significance. The spleen extended 3 inches (7.6 cm.) below the costal border, and the liver 1 inch (2.5 cm.) below. The hemoglobin was 25 per cent, red cells 1,500,000 per cubic millimeter, and the leukocytes 14,000 with 53 per cent polymorphonuclears. There were 25 nucleated red blood cells to 100 leukocytes. The blood Wassermann reaction was 4 plus, and the spinal fluid reaction was negative.

After the transfusion of 125 cc. of the father's blood, the hemoglobin rose to 40 per cent and the nucleated red cells numbered 8 per hundred leukocytes. There were 208,000 platelets. The diagnosis of anemia due to congenital syphilis was made, and the child was discharged improved after the transfusion. She returned a month later because the mother reported that the child had fever occasionally, and that there had been one epistaxis. The spleen was firm and palpable 8 cm. below the costal margin. The blood showed 30 per cent hemoglobin, 1,500,000 red blood cells, 17,000 leukocytes, 41 nucleated red cells per hundred leukocytes and 288,000 platelets. The blood gave a 2 plus Wassermann reaction. The icterus index was 8.3. The condition remained about the same in spite of treatment with neoarsphenamine. Splenectomy was performed by Dr. Bolling on Sept. 10, 1924. She did well after the operation, but her blood showed practically no improvement. The nucleated red cells increased up to 608 per hundred white cells. She was discharged in fair condition and was readmitted four months later with an attack of bronchopneumonia from which she recovered. She died at home of bronchopneumonia two years and three months after splenectomy.

CASE 7.—L. S., a white girl, aged 11 months, was brought to the Babies' Hospital because she had been losing weight and growing paler for four months. The spleen extended almost to the iliac crest and was firm. The liver reached 4 cm. below the costal margin. The cervical glands were enlarged, and there was a hemic murmur. Examination of the blood showed that the hemoglobin was 20 per cent, the red cells 2,080,000, the leukocytes 14,200 with 65 per cent polymorphonuclears, 27 lymphocytes, 7 monocytes and 1 eosinophil. There were 207 normoblasts to 100 white cells. The bleeding time was four minutes and the coagulation time four and a half. Two days later, the red cells had dropped to

1,700,000 and the white cells to 9,490. The differential count was about the same and the normoblasts had increased to 499 per hundred leukocytes or 45,320 per cubic millimeter. The red cells showed achromasia, polychromasia, poikilocytosis, Howell-Jolly bodies, Cabot rings and stippling. Some normoblasts showed dividing nuclei. The delayed, direct van den Bergh reaction was 2 plus and the indirect also 2 plus. After transfusion the red cells rose to 3,250,000 and the normoblasts fell to 203 per hundred leukocytes. One month later they had dropped to 97, and the leukocytes numbered 10,870 with 3 per cent myelocytes and 1 per cent myeloblasts. The child left the Babies' Hospital ten days after admission, and was followed for two months in the follow-up clinic. She entered St. Mary's Hospital, where splenectomy was performed nine months later. She was discharged improved after one month but was readmitted and given transfusion in another month. She died about a year after splenectomy. Through the courtesy of Dr. Byard, a piece of the spleen was given us for microscopic examination. It showed rather more myelinization than any of our other specimens. The malpighian bodies were small, and the sinuses contained blood cells with many nucleated red cells among them. A family history could not be elicited in this case.

CASE 8.—A. L., a girl of Italian parentage, aged 7½ months, was admitted to the Babies' Hospital because of marked anemia. The family history was unimportant. The blood showed: 3,000,000 red cells with a hemoglobin of 45. The leukocytes were 17,000, with 16 per cent polymorphonuclears. Many nucleated red cells were present. The Wassermann reaction was negative. The spleen reached 6 cm. below the costal margin, and the liver 4 cm. below. The icteric index was 16.6. The child was moderately rachitic. Transfusion with the mother's blood was done without influencing the blood picture.

She was readmitted four months later with a hemoglobin of 40 per cent, 2,500,000 red cells and 22,000 leukocytes. Of these, 45 per cent were polymorphonuclears, 44 per cent were lymphocytes, 9 per cent were monocytes, 1 per cent eosinophils and 1 per cent basophils. Thirteen nucleated red cells and 2 myelocytes were counted to 100 leukocytes. Stippling of the red cells was present. After transfusion, the red cells rose to 3,700,000 and the nucleated red cells increased to 31 per hundred leukocytes. The icteric index fell to 10. The child was discharged and followed in the clinic for several months during which her condition remained the same. She died at home when she was 3 years old.

CASE 9.—M. N., a girl of Italian parentage, aged 8 months, was admitted with a history of having been pale since birth and not gaining weight. The family history was unimportant. The hemoglobin was 18 per cent, the red cells 1,032,000 and the white cells 31,100. There were 42 nucleated red cells counted to 100 leukocytes. There was a hemic murmur at the apex; the spleen extended 10 cm. below the costal margin and the liver 6 cm. below. The Wassermann reaction was negative. In spite of three transfusion, the child's blood picture did not improve, although the red cells rose for a time. She died at home at the age of 21 months.

COMMENT

The points of similarity in this group of cases are: first, the familial history in five; second, the blood picture before operation; third, the blood picture after operation; fourth, the histology of the spleen; fifth, the progressive course and the fatal ending in all but one.

The presence of malaria, *Leishmania* or any other form of parasite can be definitely excluded, because repeated examination of the blood,

stools and sections of the spleen gave negative results. Five of the children were moderately rachitic, and one was syphilitic. None gave evidence of tuberculosis.

The ages of the patients ranged from 7 months to 4 years when first seen and from 13 months to 4 years and 7 months when splenectomy was performed. Six were girls and three were boys.

Familial History.—B. and N. S. were brother and sister. They showed a similar blood picture, but the anemia of the boy began in the second half of his first year, while the girl was said to have been well until the second half of her second year. An older brother died in another institution about a year after splenectomy.[2] A younger child, born after the death of N., was brought for examination of the blood when several weeks old, and again at the age of 1 year. Her blood was quite normal, and her spleen not palpable. Both parents had normal blood counts.

F. and V. P. were brothers in whose family three other children were said to have died of anemia. These children lived under good hygienic surroundings and were given intelligent care.

S. G.'s family history shows that an older child died after exhibiting similar symptoms, pallor and loss of strength.

C. M.'s family history reveals no similar case. She is the only one in whom serologic examination showed the presence of syphilis.

As far as could be ascertained, no instance of anemia in the older generations of these families existed.

Blood Picture before Operation.—Pallor was the symptom stressed by the parents, and the color on admission was stated as sallow, lemon yellow, or pale, but not jaundiced. The hemoglobin varied from 18 to 45 per cent, the red cells from 1,500,000 to 3,500,000, leukocytes from 9,000 to 50,190 and the nucleated red cells from 7 to 207 per hundred leukocytes. Fragility of the red cells was within the normal range. The platelets were normal in number except in the case of B. S., in which they were low for a time, but later rose to normal. Urobilinogen in the stools and urine was increased in the four cases in which it was studied.

Blood Picture after Operation.—After splenectomy the blood gave the characteristic picture of a definite and progressive increase in the nucleated red cells, most of which were normoblasts. They ranged from 148 to 2,016 per hundred leukocytes, or from 1½ to 20 times as many. Two of the patients survived splenectomy four years, and in both, one being still alive, the nucleated red cells became not only more numerous but more immature. Thus the blood of B. S. (fig. 6) showed normoblasts, megaloblasts with polychromatic cytoplasm and mitotic nuclei, reticulocytes, and Howell-Jolly bodies. The mature red cells showed

most marked poikilocytosis and anisocytosis, polychromasia and friability of the cell bodies.

The hemoglobin and the total number of red cells remained below normal. The number of leukocytes diminished but little; the monocytes were increased for several weeks and then fell to normal.

The blood of three other patients on whom splenectomy had been performed for hemolytic jaundice, essential thrombopenia, and Banti's disease, was followed for from three to seven years after operation. None showed the presence of nucleated red cells after the first few weeks, and never in such numbers as did these patients with von Jaksch's anemia.

Histology of the Spleen.—The spleen was ten times heavier than normal in the youngest patient, and from four to seven times in the older ones. The size and weight are given in table 2.

TABLE 2.—*Data of Splenectomy in Six Cases*

Age	Size of Spleen, Cm.	Weight of Spleen, Gm.	Survival after Splenectomy
S. G. 4 years	11.5x9	170	4 years
C. M. 3½ years	15x9.5	267	2 years
F. P. 3¼ years	14x10.5	231	5 months
B. S. 2 years	13x8	192	over 4½ years
N. S. 1 year	15x10	224	4 months
L. S. 1¾ years*			1 year

* Splenectomy was performed at St. Mary's Hospital and we are grateful to Dr. Byard for notes of the history after the child had left the Babies' Hospital and for material from the spleen.

The capsule was thickened over the outer border in two, and in the case of C. M. over the entire organ, with a dense scar near the upper pole. Adhesions between the spleen and the stomach are mentioned in case 5. On section, the septums were found thickened in the case of C. M., whose Wassermann reaction was positive. The malpighian bodies were visible to the naked eye in the spleen of the two oldest patients. An interesting point is the presence of supernumerary spleens in four of the five children, varying in number from two to seven and in size from 2 mm. to 1 cm. in length. In the case of N. S., who came to autopsy five months after splenectomy, one supernumerary spleen had reached the size of 3.5 cm. in length and the weight of 6 Gm., while a second was only 1 cm. long.

Microscopically, also, the picture was similar. There was a mild general fibrosis, the sinuses were wide, partly empty and partly filled with blood cells, and myelogenous areas were present. The vessels were not unduly filled with red cells, and their walls were normal. The splenic reticulum was thickened. The malpighian bodies were not numerous. Iron pigment was found in the sinuses and in their lining cells, but not in the septums. Myelinization was expressed by the

presence of eosinophilic myelocytes, nucleated red cells and myeloblasts. The picture varied slightly, myelogenous areas being few and small in three, and larger in three. The connective tissue septums and the capsule were thickest in the spleen of C. M., whose blood gave a positive Wassermann reaction. They were not thickened in case 1. In the only case which came to autopsy, myelogenous foci were found in the liver, and two supernumerary spleens not removed at operation had become enlarged.

Progressive Course and Fatal Ending.—The onset of the anemia was given as soon after birth in two instances. It was definitely stated by the parents as occurring at the end of the first half year of life in five children, in the second half of the second year in one and in the third year in one. In all the spleen was enlarged at the first examination, and its lower border was found at a point varying from 6 cm. below the costal margin to the crest of the ileum. The liver was moderately enlarged in all, extending from 1 to 7 cm. below the costal border. There was a general, though moderate, adenosis in seven. Jaundice was mild or not present, and the icteric index was within normal range in five of the seven children on whom the test was done. In one it was 16.6, indicating a beginning jaundice. In case 4, the patient had a lemon yellow color and an icteric index of 25 three years after splenectomy, due to marked hemolysis. The van den Bergh test gave a delayed direct reaction, indicating increased hemolysis; this was also borne out by increased urobilinogen in the stools in cases 3 and 4. Epistaxis occurred in one patient, but no other hemorrhages were noted. The course was chronic, lasting from five months to three years before splenectomy, and from four and one-half months to more than four and two-thirds years after splenectomy, as evidenced by the blood picture and the changes in the bones demonstrable on roentgen examination.

The oldest boy, S. G., had the Mongolian features first noted by Cooley [1] and shown in figure 1, taken one month before he died. His long bones showed rarefaction.[3] C. M.'s bones showed no change, and B. S. showed more rarefaction in 1929 than in 1928. Her features are but slightly altered. Control pictures of children with leukemia failed to show similar changes in the bones.

The changes in the bones in these cases would seem to be explained by the experiments described by Johnstone,[4] who found enlargement of the marrow cavity through an actual thinning of the compact bone

3. Cooley, T. B.; Witwer, E. R., and Lee, Pearl: Anemia in Children with Splenomegaly and Peculiar Changes in Bones, Am. J. Dis. Child. **34**:347 (Sept.) 1927. Whipple, A. O.: Atypical Hemolytic Anemia with Splenomegaly in Children, Ann. Surg. **88**:380, 1928.

4. Johnstone, E. M.: Changes in the Morphology and Function of the Bone Marrow After Splenectomy, Arch. Surg. **5**:159 (July) 1922.

in the dog during increased formation of red cells after splenectomy. Brannan [5] described the gross and microscopic appearance of the frontal bosses in a case of von Jaksch's anemia, but gave no roentgenograms, such as were first published by Cooley, Witwer and Lee [6] and then by Whipple.[7] Brannan's [5] description said that the frontal and parietal bosses were large and hard. Microscopically, the outer table was thin, "with small and fragmented bone lamellae, the delicate fibrous tissue of the marrow most abundant under the outer table." Hyperplasia of the marrow seems to cause the changes in the bones.

A diagnosis of von Jaksch's anemia was made in these cases because they seemed to fit into the picture made by the descriptions of von Jaksch,[8] Hayem,[9] Luzet,[10] Stillman [11] and Cooley.[12] In von Jaksch's [8] first paper, he described an anemia with enlargement of the spleen, liver and lymph nodes accompanied by a high leukocytosis of long duration, but without the lesions of leukemia at autopsy. As differential points, he said that the liver increased in size less rapidly than the spleen and that the prognosis is not so bad as in leukemia, since he saw at least one patient who recovered. He called the condition anemia infantum pseudoleukemica. In the following year, he [13] described a fatal case in a girl, aged 11 months, whose hemoglobin was 15 per cent, red cells 800,000 and leukocytes 54,666. She had a large spleen, but the liver was not enlarged. At autopsy the diagnosis was anemia gravis, rickets, chronic spleen tumor, fatty degeneration of the heart and chronic pulmonary edema. Microscopically, the spleen pulp contained leukocytes carrying pigment and pale red cells. Syphilis was not present, and von Jaksch stated that the condition may occur in nonrachitic children.

He also detailed the case of a child, aged 19 months, who recovered rapidly after treatment with iron, although the red cells had fallen as low as 1,380,000 and the white cells had ranged between 43,333 and

5. Brannan, Dorsey: Extramedullary Hematopoiesis in Anemia, Bull. Johns Hopkins Hosp. **41**:104, 1927.

6. Cooley, Witwer and Lee (footnote 3, first reference).

7. Whipple (footnote 3, second reference).

8. Von Jaksch, R.: Ueber Leukemie und Leukocytose im Kindesalter, Wien. klin. Wchnschr. **2**:435 and 456, 1889.

9. Hayem: Du Sang, Paris, 1889.

10. Luzet, C.: Etudes sur les anémies de la première enfance et sur l'anémie infantile pseudo-leucémique, Thèse de Paris, 1891.

11. Stillman, R. G.: A Study of von Jaksch's Anemia, Am. J. M. Sc. **153**:218, 1917.

12. Cooley, T. B.: Likenesses and Contrasts in the Hemolytic Anemias of Children, Am. J. Dis. Child. **36**:1257 (Dec.) 1928.

13. Von Jaksch, R.: Ueber Diagnose und Therapie der Erkrankheiten des Blutes, Prag. med. Wchnschr. **15**:387, 403 and 414, 1890.

114,150. Finally, for contrast, he described a case of anemia due to pneumonia with a leukocytosis of 36,000. Von Jaksch did not mention nucleated red cells, but Hayem [9] studied a case in Paris and described nucleated red blood cells with karyokinetic figures. His pupil Luzet [10] made the subject of his thesis "Etudes sur les anémies de la première enfance et sur l'anémie infantile pseudo-leucémique," in which he collected reports of six cases, two of which were his own, with one autopsy. Luzet found hematopoiesis in the spleen and liver. He thought that some cases go on to recovery while others develop into true leukemia, a view which modern observations have disproved.

Taking the description of von Jaksch, Hayem and Luzet together, we have an anemia in infants and young children characterized by low hemoglobin and red cell content, high leukocytosis, nucleated red cells continually present in abnormal numbers, an enlarged spleen, a liver that may be normal or moderately large, rickets not always present, and a prognosis which is bad but not invariably fatal. At autopsy both liver and spleen show areas of hematopoiesis. The introduction of splenectomy as a cure for anemia of this type brought out the characteristic postoperative blood picture first recorded by Stillman [11] and then by Cooley.[1] Stillman found that the nucleated red cells in his first patient (aged 10 years) increased to 25 times the number of leukocytes after splenectomy, then fell to 5 times as many and two years later numbered 138 to 100 leukocytes. Hitzrot [14] reported on this same case fourteen years after splenectomy, when there were still 5 times as many nucleated red cells as leukocytes. Stillman thought that the essential changes seemed to be in the erythropoietic system, a fact that Cooley emphasized again and therefore suggested the name "erythroblastic anemia of childhood." Cooley [6] added a further characteristic to the clinical picture when he described the gross and roentgenographic changes in the bones in these cases. It is interesting that Gänsslen [15] had called attention to the negroid type of features in certain cases of familial hemolytic icterus, though no roentgen studies were made.

The question of diagnosis presented many interesting points. The familial character suggested hemolytic icterus. Neither the normal fragility nor the absence of jaundice contraindicated that diagnosis, but the blood picture before and after splenectomy ruled it out. It was clearly not an anemia due to bad nutritional habits, nor did the removed spleen show the histologic picture of Banti's disease which the absence of hemorrhages and the early age of the children also made

14. Hitzrot, J. M.: Unclassified Type of Splenomegaly in Children, Ann. Surg. **88**:361, 1928.

15. Gänsslen, M.: Die haemolytische Konstitution, Deutsches Arch. f. klin. Med. **146**:1, 1925.

remote. Finally, the therapeutic failure of splenectomy proved that the condition is not hemolytic icterus. We have been able to follow the increase in reticulocytes after liver therapy in cases of anemia resulting from wrong nutrition, and therefore we do not feel that such changes justify a diagnosis of pernicious anemia in an infant. Peabody's [16] studies showed that pernicious anemia is a disease of the bone marrow with proliferation of megaloblasts and lack of maturation to normal red cells. This fact has been emphasized and further proved by Minot [17] in his studies on pernicious anemia with liver therapy. We have not been able to study marrow in our cases, because at the Babies' Hospital bone puncture is not considered a permissible procedure in young children, and our only specimen was obtained at autopsy four months after splenectomy. However, it would seem that in von Jaksch's anemia there is a profound marrow lesion with red cell maturation arrested at the normoblastic stage, a stage that is more mature than that of the megaloblast and so possibly more compatible with function and with life. That the lesion is a progressive one, more immature cells gradually appearing in the circulation, is shown by our patient B. S. Since maturation of the red cells is apparently accomplished by liver therapy, the treatment is now being given to B. S.

The prognosis, in our experience, is bad; though the patient may survive splenectomy for five years, the disease is not cured. Hitzrot's patient was alive fourteen years after splenectomy.

SUMMARY

It seems to us that the anemia described by von Jaksch and Hayem, when studied in the light of present hematologic knowledge, is a definite clinical entity, which has a familial history in many cases, a definite blood picture, changes in the long bones and in the flat bones of the skull, a chronic course and a bad prognosis, and is not cured by splenectomy.

16. Peabody, F. W.: The Pathology of the Bone Marrow in Pernicious Anemia, Am. J. Path. **3**:179, 1927.

17. Minot, G. R.: Treatment of Pernicious Anemia with Liver Extract; Effect upon the Proportion of Immature and Mature Red Blood Cells, Am. J. M. Sc. **175**:559, 1928.

CONGENITAL COMPLETE HEART BLOCK

REPORT OF A CASE WITH AN ASSOCIATED PATENT DUCTUS ARTERIOSUS *

CLIFTON B. LEECH, M.D.
BALTIMORE

The following case is reported because it represents an addition of an uncommon condition to the reported cases, emphasizes the ease with which such a case may escape recognition and indicates the importance of electrocardiographic study, includes a striking and characteristic roentgenogram, and offers an interesting combination of congenital defects which fail to give rise to markedly characteristic symptoms or physical signs.

REPORT OF CASE

History.—D. D., a white girl, born on Nov. 5, 1918, was first seen in the Harriet Lane Dispensary on Jan. 23, 1924, at the age of 5½ years, with a complaint of languidness, nervousness, jumping of the heart and swelling of the neck. The family history was unimportant and there was no knowledge of syphilis. A sister, aged 3½ years, and a brother, aged 17 months, were living and well.

The past history included a normal, full-term delivery, with no snuffles, desquamation or cyanosis during infancy. The birth weight was 5¾ pounds (2.6 Kg.). The child was fed breast milk for one year; during the second year she was given condensed milk with soft foods. Since the age of 3 years she had had a poor appetite.

Development at this time seemed comparatively normal; she sat up at the age of 3 or 4 months, talked at from 12 to 15 months and walked at 16 months.

Diseases included bronchitis at the age of 15 months, measles at 2 years, chickenpox at 3 and pertussis at 4½.

Examination.—Nothing remarkable was noted during the physical examination except hypertrophic tonsils, acute cervical adenitis and a slight enlargement of the heart with a rough systolic murmur over the precordium. A slow pulse was attributed to the effect of digitalis which the child had been given by a private physician.

On a number of occasions at the dispensary, various routine examinations, including tuberculin tests, gave negative results.

Course.—In March, 1924, the patient was admitted to the hospital for further study of the cardiac condition, since a congenital malformation was suspected. During her stay in the hospital, a description of the murmur was essentially the same as the one which will follow. At this time a clear third heart sound was heard. It was concluded that the congenital malformation was a patent interventricular septum. Several consultants saw the patient, but apparently a heart block of any degree was not seriously considered. The patient contracted scarlet fever followed by nephritis. She was discharged in June, 1924, with no evidence of nephritis and with no change in the condition of the heart.

* Submitted for publication, June 15, 1929.

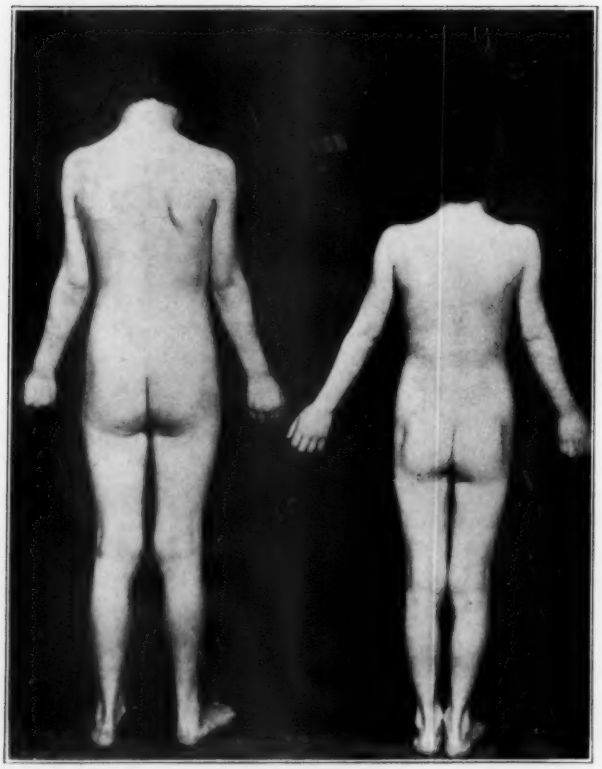

Fig. 1.—D. D. photographed with her seven months older, normally developed cousin.

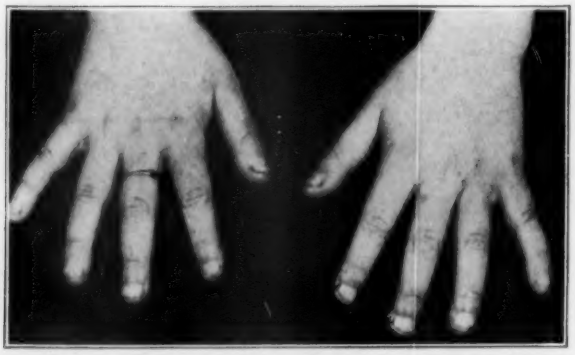

Fig. 2.—Noticeable thickening at bases of the nails in the case reported, a sign sometimes observed in children with cardiac disease even in the absence of other signs of circulatory congestion. The stretched skin at the thickened bases of the nails gives a glistening appearance.

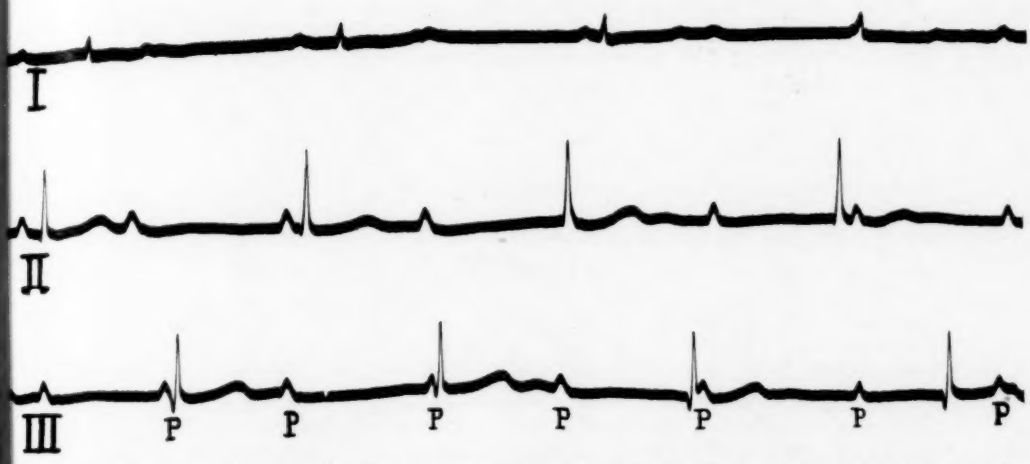

Fig. 3.—Electrocardiogram, showing complete auriculoventricular dissociation. Auricular rate 75, ventricular rate 37. The apparent sinus arrhythmia may be accounted for by the fact, shown by Canby Robinson, that the P-P intervals, which include a ventricular deflection, are often shorter than the other P-P intervals. I, II and III indicate the leads.

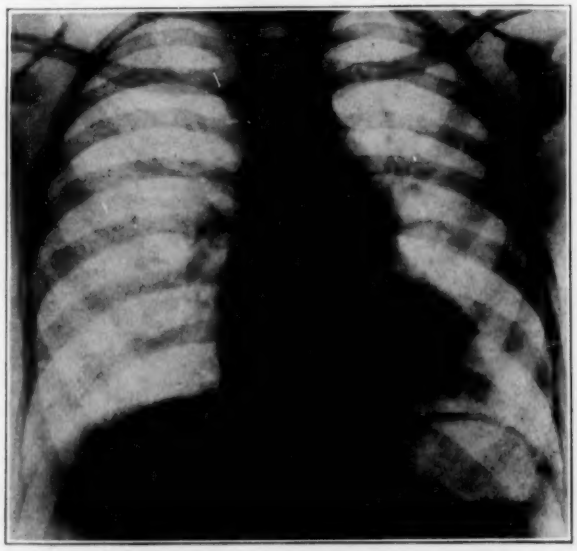

Fig. 4.—Teleoroentgenogram, showing dilated conus characteristic of patent ductus arteriosus.

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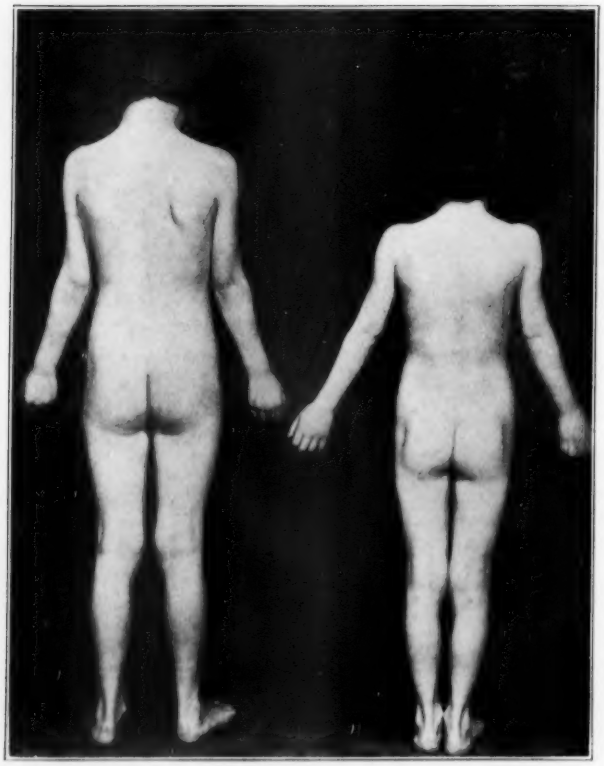

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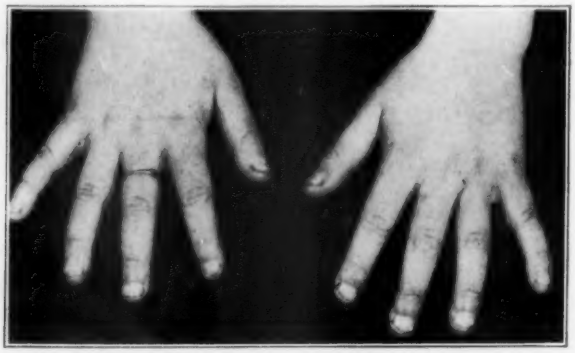

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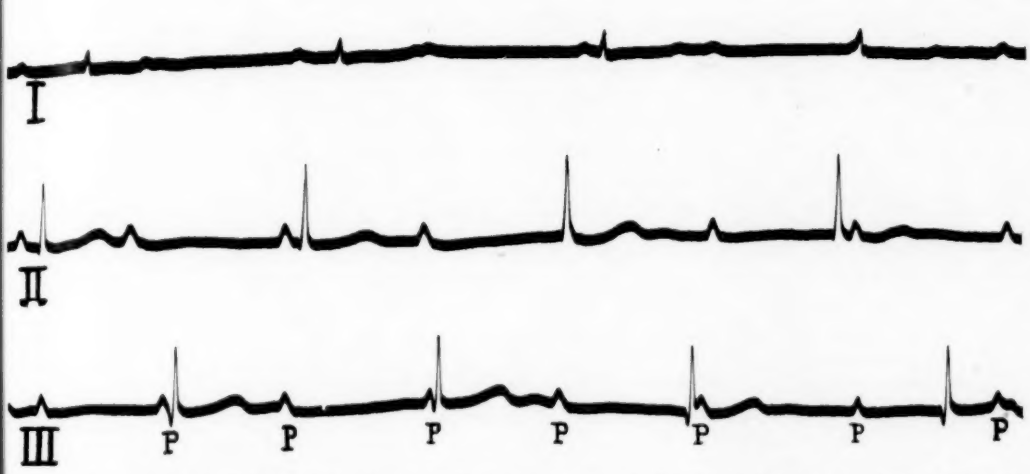

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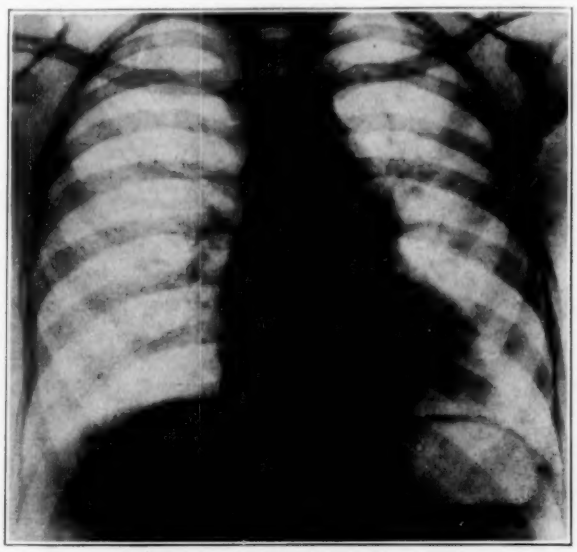

Fig. 4.—Teleoroentgenogram, showing dilated conus characteristic of patent ductus arteriosus.

In August, 1924, her tonsils were removed. During 1925, she spent several months at a convalescent home for children. In the early part of 1926, she developed measles for the second time and was sent to a hospital for contagious diseases where she also suffered from pneumonia. Shortly after her return home she developed acute otitis media and a discharge from the vagina. She returned again to the Harriet Lane Dispensary and was treated in various clinics until the vaginitis and the bilateral otitis media cleared up, in October, 1926. She was then followed from time to time in the Gynecological Clinic and was not seen in the Harriet Lane Dispensary until June, 1928, at which time a careful physical examination gave no evidence of nephritis. The phthalein excretion was 70 per cent the first hour and 10 per cent the second hour. The blood showed: nonprotein nitrogen, 29 mg. per hundred cubic centimeters; creatinine, 1.2 mg.; chlorides, 509 mg.; uric acid, 2.4 mg., and hemoglobin, 88 per cent; the blood pressure was 85 systolic and 60 diastolic. There was a negative reaction to tuberculin. The fundi were normal. At this time a teleoroentgenogram showed an atypical shaped heart.

The patient was next seen during November, 1928, in the Cardiac Clinic of the Harriet Lane Dispensary where she was examined by Dr. Bernard Benjamin who suggested that the pulse rate of 48 might be due to heart block. After exercise, the pulse rate increased to 63. Such a response was thought to consti-

Measurements of the Cardiac Dulness

	Right, Cm.	Left, Cm.
I	1.5	2.5
II	1.5	3.0
III	2.5	2.25
IV	2.5	6.0
V	3.5	7.0
VI	3.5	6.0

tute evidence against the likelihood of there being a high degree of block, but an electrocardiogram showed the presence of complete auriculoventricular dissociation. This led to further study of the patient. It was again noted that she was slightly deaf and distinctly underdeveloped. She was seen in the laryngological department where it was felt that the inner ear type of deafness was not due to congenital abnormality. The lips, tongue and buccal mucous membrane were normally pink. The nails were blue only when the extremities were cold. There was no clubbing of the fingers or toes, but thickening at the bases of the nails was visible. There was no capillary pulsation. Nodules, petechiae and rash were absent. The teeth were not infected; the gums were normal. The pharynx was clean, without tonsils. There were small tonsillar nodes and small palpable cervical glands. Moderate asymmetry of the anterior thoracic wall with bulging of the left precordium and a slight scoliosis of the thoracic spine were observed. No abnormal pulsations were detected in the chest, but regular systolic pulsations were seen in the vessels of the neck on either side and in the suprasternal notch. Between these pulsations and at times overlying them were definitely visible venous pulsations. A faint and fine thrill, systolic in time, was felt over the base of the heart, especially in the second and third interspaces, and over the vessels of the neck on either side, especially on the left. This thrill was not always felt; it was entirely absent at some examinations. No thrill was felt at the apex. The apex impulse was rather diffuse but was maximal in the fifth space, 7 cm. to the left. The measurements of cardiac dulness are given in the accompanying table.

The heart sounds at the base were moderately loud; the pulmonic second sound was definitely accentuated. At the apex both sounds were slightly louder than normal with a moderate accentuation of the first sound. The third sound was easily heard early in diastole at the apex. A systolic murmur of moderate intensity and of a blowing quality was heard over the entire precordium with about equal intensity at the base and apex. Its maximum intensity was in the third and fourth interspaces, more particularly in the fourth, left, close to the edge of the sternum. In this particular area the murmur had a harsher quality. The murmur was only faintly heard outside the area of cardiac dulness and was not heard at all in the left axilla or back. It was heard slightly better with the patient in a reclining position and lying on the left side. Over the carotid vessels on either side of the neck, and below the inner third of the clavicles, a continuous humming murmur was heard. Pressure by the stethoscope on the jugular veins did not affect the intensity of this murmur. A moderately faint pistol shot was heard over the femoral vessels. The radial pulses were equal and small and were not otherwise remarkable. The blood pressure in the upright position was 90 systolic and 60 diastolic. There was no pulse deficit. The liver and spleen were not palpable. There was no evidence of circulatory congestion, but a few medium and fine moist râles were scattered throughout the chest. The heart rate was 52 and regular. It was increased by exercise (hopping for thirty seconds) to 64. Exercise intensified the murmur but did not seem to influence the thrill. The vital capacity determination was unsatisfactory because of lack of cooperation by the patient. Ocular pressure slowed the pulse rate slightly. Examination of the blood gave a leukocyte count of 8,700, with 66 per cent polymorphonuclear neutrophils, 10 per cent large lymphocytes, 18 per cent small lymphocytes, 6 per cent monocytes, 5,100,000 erythrocytes and 95 per cent hemoglobin. The Wassermann reaction of the blood was negative. Electrocardiograms were taken before and after the administration of atropine and, later, after that of epinephrine. Before the application of atropine the auricular rate was 79, the ventricular, 47. Ten minutes after the administration of atropine (1/150 grain [0.00195 Gm.]) the auricular rate was 73, the ventricular, 57. Twenty minutes after the application of atropine the auricular rate was 115, the ventricular, 79, still with complete A-V dissociation. Epinephrine produced essentially the same effect, an increase in both the auricular and the ventricular rates, without disturbance of the complete A-V dissociation.

COMMENT

The effect of atropine and epinephrine in stimulating both auricles and ventricles to increased activity seems to be rather unusual. The use of atropine is reported in seven of the cases in the literature and in only one instance were the ventricles accelerated. In that case, as well as in mine, the complete dissociation still held. Few of the authors reported the use of epinephrine. The effect of both the atropine and the epinephrine in my case in increasing the ventricular rate, as well as that of the auricle, is thought to be due to the paralysis of the vagal fibers in the auricle and in the area adjacent to the focus giving rise to the idioventricular rhythm after the use of atropine, and to the effect of epinephrine on the sympathetic endings. Such an interpretation seems reasonable in view of the fact that complete dissociation was in no way disturbed, the ventricular complexes were unchanged in

contour and the marked response of the ventricles to exercise showed an easily excitable focus of idioventricular activity. This, with vagal and sympathetic effects, accounts for the fact that the pulse rate was seldom the same at successive examinations.

The teleoroentgenogram presents a striking shadow which can be interpreted in three possible ways. The most likely interpretation is that of a dilated pulmonary conus due to a patent ductus arteriosus. This shadow represents a bulging of the first left arc, whereas a dilatation of the left auricle produces a bulging of the second left arc. Fluoroscopic examination seems to be confirmatory of this interpretation for the dilated conus was readily visible and was seen to fill with ventricular systole, while the auricular contractions could be seen at an independent and enhanced rate. An associated interventricular septal defect is not ruled out. The second possible explanation is that the shadow is produced by a dilated pulmonary arc with hypertrophy of the right ventricle associated with a defect in the interventricular septum. The fluoroscopic evidence is against this, for, in the lateral view, the right ventricle did not seem to be hypertrophied. The third possible cause of this striking shadow is dextroposition of the aorta associated with a septal defect.

That this complete block is congenital in origin seems certain in the absence of typical precardiac disease or of disease which is known to produce heart block. Because of the variability of the pulse rate with its misleading and comparatively rapid action at times, a graphic study of the heart beat was not made earlier. The association of the block with other congenital stigmas is further evidence. There are no physical signs which by themselves could be considered definitely to indicate a congenital anomaly. The murmur itself is not characteristic, and the venous hum in the vessels of the neck is sometimes heard in normal children, but the presence of the basal thrill and the roentgenographic and fluoroscopic evidence combine to establish the diagnosis of patent ductus arteriosus. There may be also a defect in the interventricular septum, although the evidence for this is inconclusive and dependent partly on the presence of the congenital complete heart block.

REVIEW OF LITERATURE

Davis and Stecher [1] recently reviewed the literature and tabulated twenty cases of heart block, proved by graphic records, of undoubted congenital origin, sixteen of which were of the complete auriculoventricular dissociation type. They reviewed a number of other reports

1. Davis, Hart; and Stecher, R. M.: Congenital Heart Block: Report of Additional Case, with Review of the Literature, Am. J. Dis. Child. **36**:115 (July) 1928.

of probable congenital heart block. They emphasized the lack of serious complaint in these patients in view of such a marked circulatory disorder and noted the frequency with which this condition is associated with other congenital abnormalities of the heart. Since Davis and Stecher's review of the literature, there have been a number of other case reports published. Aylward [2] reported two probable cases occurring in the same family. One other probable case was reported by Haverschmidt.[3] Fleming and Stevenson [4] reported in children two cases of undoubted congenital heart block proved by an electrocardiogram. One was an instance of complete A-V dissociation, and the other of 2-1 block. These authors considered congenital heart block to be confined probably to cases in which there is a defect in the interventricular septum and in which there is an associated maldevelopment of the A-V bundle. They explained that the reason why more cases of septal defect, which is a common deformity, do not also exhibit block is that the usual site of the defect is anterior to the pars membranaca while the A-V bundle lies behind it. However, the well known observations by Keith, Abbott, Morison and others indicate that the bundle emerges from the A-V node, close to the interauricular septum behind the medial cusp of the tricuspid valve; the left branch of the bundle pierces the interventricular septum in front of the pars membranaca and passes down superficially beneath the septal endocardium to the papillary muscles and the columnae carneae of the left chamber, while the right branch runs more deeply embedded in the musculature of the right side of the septum to the apex of the right ventricle.

Lampard,[5] in a recent review of the literature, accepted thirty-one cases as representing true congenital block though some of these were not proved by electrocardiograms. Several were of possible syphilitic or diphtheric origin. Lampard concluded that congenital heart block is usually associated with an anomaly of the interventricular septum but is not due so much to a defect in the septum as to the presence of fibrous tissue causing pressure on the bundle of His. He stated that when there is a defect in the septum the bundle may run along the edge and is liable to be damaged by inflammation from rheumatic fever, syphilis and diphtheria. He reported an autopsy which revealed the complete absence of the interventricular septum with the presence of the A-V bundle, the block being due to fibrous tissue in the A-V bundle. He expressed the belief that pressure on the bundle plays a greater part in production of the block than partial destruction plays. This is

2. Aylward, R. D.: Brit. M. J. **1**:943 (June 2) 1928.

3. Haverschmidt, J.: Nederl. Tijdschr. v. Geneesk. **1**:1166 (March) 1928.

4. Fleming, G. B., and Stevenson, M. M.: Heart Block Associated with Congenital Malformation of the Heart, Arch. Dis. Childhood **3**:221 (Aug.) 1928.

5. Lampard, M. E.: Arch. Dis. Childhood **3**:212 (Aug.) 1928.

sound, since it is well known that a single strand may convey impulses. He cited instances of partial block of the congenital type which became of a higher degree, or even complete, at inspiration, when the heart is in a more vertical position and there is greater tension on the septum. Apropos of this, an extremely interesting case is reported by Smith [6] who published electrocardiograms of a normal sequential rhythm only at forced complete respiratory expiration; at all other times block was present.

Davis and Stecher [1] suggested that congenital block may be due to failure of development of the conducting system. In this connection it would seem that block due to such developmental anomalies would be likely to cause an exhibition of abnormal ventricular complexes in the electrocardiogram. If there were defects of development in the conducting fibers sufficient to produce a high grade or complete block it would seem to be unlikely that the idioventricular focus of impulse would be consistently situated sufficiently high in the bundle to produce normal ventricular complexes in the electrocardiogram. Carter and Howland [7] mentioned the well known fact that the evolution of the His-Tawara bundle results from the growth downward of the primitive cardiac tube with a gradual severance of muscle continuity between auricles and ventricles except for the narrow strand which is later differentiated as the atrioventricular bundle. They conceived that abnormal development at such a time may involve only that group of cells which later is to become the A-V node or upper part of the main stem to a widely varying degree. Granting the reasonableness of this conception, it still seems to me that such a defect in development would be likely to result in the abnormal complexes aforementioned. It seems unlikely that developmental defects of the conducting fibers would be confined almost entirely to the origin of the bundle rather than to its main stems and arborizations, defects which should produce bizarre ventricular complexes. A study of the published electrocardiograms of cases of congenital heart block reveals the following data.

Including the present case there are fourteen electrocardiograms [8] published of complete block of probable congenital origin. In another [9]

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6. Smith, S. C.: High Grade Heart Block, J. A. M. A. **76**:17 (Jan. 1) 1921.

7. Carter, E. P., and Howland, J.: Bull. Johns Hopkins Hosp. **31**:351 (Oct.) 1920.

8. Rosenson, W.: Arch. Pediat. **39**:567, 1922. White, P. D.; Eustis, R. S., and Kerr, W. J.: Congenital Heart Block, Am. J. Dis. Child. **22**:229 (Sept.) 1921. McIntosh, R.: Congenital Heart Block: Report of Case, Am. J. Dis. Child. **34**:965 (Dec.) 1927. Whipham, T. R.: Brit. J. Child. Dis. **12**:321, 1915. Wilson, J. G., and Grant, R. T.: Heart **12**:295 (March) 1926. Gorter, E. M.: Nederl. Maandschr. v. Verlosk. **8**:377, 1919. Calandre, L.: Arch. de cardiol. y hematol. **2**:225 (June) 1921. Footnotes 1, 4, 6 and 7.

9. Bass, M. H.: Heart Block, J. A. M. A. **70**:287 (Feb. 2) 1918.

there are ventricular complexes of sinus node origin as well as complexes of normal contour from an idioventricular focus. One electrocardiogram [10] showed split QRS complexes in lead I. In four reports,[11] the electrocardiograms were not published but had been made. They were not described as showing abnormal ventricular complexes. This seems to be rather strong evidence against the congenital block being due to developmental defects of the conducting system per se. Since the ventricular complexes, which are a result of transmission of impulse through the Purkinje system, are normal in contour the impulse which gives rise to them must be developed in the course of the main bundle above the bifurcation. It follows that the lesion responsible for the block must be above this level, comparatively close to the auriculoventricular septum.

Patent ductus arteriosus is a rare complicating anomaly in this series; in fact, it has not been definitely diagnosed in a single reported instance. The diagnosis was suggested in Rosenson's [10] case, was considered possible in the case reported by Romberg and White [12] and was thought to have occurred in a case reported by Willius; [13] it was thought by White, Eustis and Kerr [14] that the case reported by them was one of patent ductus arteriosus. In the last case a complete block, noted at the age of 4 days, disappeared when the child was 8 months old. This seems to be additional evidence in favor of pressure effects in the etiology of block in some of these cases. The case herein reported seems to be the first in which there can be slight doubt concerning the diagnosis of patent ductus arteriosus.

In only four reported cases was there failure to mention associated lesions of the heart. Clubbing of the fingers occurred only in one or two instances. One autopsy was described in full. The published electrocardiograms showed four [15] with dextrogram predominant, one [10] with levogram predominant, the others with no axis deviation.

Prognosis cannot be definitely analyzed from the reported cases because death is mentioned only in one or two instances, but a consideration of the ages of the patients reveals that the oldest reported was 23, two were 20, two 18, two 15, two 12, one 10 and the other all under

10. Rosenson (footnote 8, first reference).

11. Romberg, E. C., and White, P. D.: Boston M. & S. J. **190**:591 (April) 1924. Gibson, Stanley: Heart Block, Am. J. Dis. Child. **34**:1090 (Dec.) 1927. Aldrich, C. A., in discussion on Gibson, Stanley: Heart Block, Am. J. Dis Child. **34**:1090 (Dec.) 1927. Barbier, Lebée and Mouquin: Soc. de Pediat., Jan. 17, 1922; reviewed in Arch. d. mal. du coeur **15**:171, 1922.

12. Romberg and White (footnote 11, first reference).

13. Willius, F. A.: Boston M. & S. J. **184**:64, 1921.

14. White, Eustis and Kerr (footnote 8, second reference).

15. Davis and Stecher (footnote 1). McIntosh (footnote 8, third reference). Whipham (footnote 8, fourth reference). Gorter (footnote 8, fifth reference).

10 years. This seems to indicate that the child with congenital heart block has a rather poor prognosis. The prognosis obviously improves, the less complicated the congenital condition; that is, the child with heart block and no other demonstrable serious defect, and with lack of symptoms, seems to deserve a much better prognosis than otherwise.

SUMMARY

A case is reported of a patient with congenital complete heart block and an associated patent ductus arteriosus. This patient presents no symptoms suggestive of complete heart block and physical signs which, lacking the roentgenographic evidence, could be said to be characteristic of patent ductus arteriosus. The report includes a characteristic roentgenogram and electrocardiogram.

The marked excitability of the idioventricular focus of activity in this case is discussed, and it is suggested that such patients may be readily overlooked.

The type of defect producing the block is discussed, and evidence is offered which suggests that congenital heart block is almost invariably due to a lesion sufficiently high above the bifurcation of the bundle of His to allow the production of normal ventricular complexes in the electrocardiogram. There is no strong evidence to indicate that this lesion is usually a defect in the interventricular septum. Study of the published electrocardiograms in cases of congenital heart block fails to reveal production by the presumed associated septal defects of a characteristic electrical axis deviation.

The prognosis in these cases is not favorable.

Direct evidence concerning the anatomic lesions is meager, and it is suggested that clinicians make special effort to obtain autopsies on the bodies of patients presenting congenital heart block.

CIRRHOSIS OF THE LIVER IN CHILDHOOD

REPORT OF A CASE OF ATROPHIC CIRRHOSIS IN A BOY AGED TEN YEARS *

T. LEONARD SUTTON, M.D.
STOCKTON, CALIF.

Cirrhosis, especially of the atrophic type, is sufficiently rare, in America at least, to justify a report of the following case.

REPORT OF CASE

History.—N. H., a boy, aged 10, was first seen in the Stanford outpatient clinic with a complaint of sores on the hands and face that proved to be impetigo contagiosa. He appeared slightly icteric, and an enlarged spleen was noted. As soon as the impetigo healed, following the usual therapy, a period of hospital observation was advised. He was in Lane Hospital for eight days in January, 1928, and was again admitted for a four day period in April, 1928.

The patient's parents were living and well. The mother had had thirteen pregnancies, the patient being the youngest child. One brother had died of heart trouble when 14 years old, and there had been one spontaneous miscarriage. The prenatal history was negative, the birth normal, and infancy and development were normal. The boy had always lived in California and had been normally healthy until June, 1927, when he had an acute gastro-intestinal disturbance with intense jaundice. The local physician gave him medicine to take by mouth that seemed to decrease the jaundice although the eyes remained slightly tinged with yellow. Except for considerable gas, slight epigastric distress at times, and a somewhat "too deeply colored yellow urine," he had been considered well.

Physical Examination.—The patient appeared rather pale and slightly undernourished, although the weight was nearly ideal. The temperature was normal. There were several moderate-sized spider angiomas on the trunk and a single large one on the right eyelid. The sclerae were slightly icteric. There were several carious teeth, and the tonsils were hypertrophied and hypercryptic. There were a few palpable anterior cervical glands. The abdomen was moderately distended, and there was a slight but noticeable increase in the abdominal venous markings. A questionable fluid wave was elicited, but no shifting dulness was found. The liver was not definitely felt, but there was considerable resistance high in the right upper quadrant. The spleen was firm, smooth and not tender, and extended 4 cm. below the left costal margin. A few dilated internal hemorrhoidal veins were felt rectally. The patient's mentality seemed normal.

Laboratory Examination.—The blood count is given in the accompanying table.

The smears showed slight changes in the shape and size of the red cells. There were 1.8 per cent reticulocytes. The bleeding time was estimated at two and a half minutes, and the coagulation time at three and three-fourths minutes. Hemolysis began at 0.42 per cent saline solution and was complete at 0.38 per cent, showing a

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* From the Department of Pediatrics, Stanford University Medical School.

decreased erythrocyte fragility. A blood clot was not dissolved after standing for twenty-four hours (Goodpasture[1] test for extreme liver damage).

The Wassermann reaction of the blood was negative.

The icteric index was 12.6, the direct van den Bergh reaction was slightly positive in twenty minutes and the indirect reaction measured 1 unit.

The routine examinations of the urine gave negative results and showed no urobilin.

Specimens of blood taken two, eight and sixteen minutes after intravenous administration of 5 cc. of 1 per cent rose bengal solution showed 100, 89 and 70 per cent of the dye still present, indicating a decreased liver function.

The stools were normal.

The gastric analysis showed no free acid in the specimen collected during fasting. This rose, however, to 12 degrees, thirty minutes after 0.3 mg. of histamine was administered subcutaneously, while the total acid rose from 6 degrees in the contents during fasting to 40 degrees, thirty minutes after the administration of histamine.

There were no reactions with 0.1 mg. and 1 mg. of old tuberculin given intracutaneously.

Blood Count of Reported Case

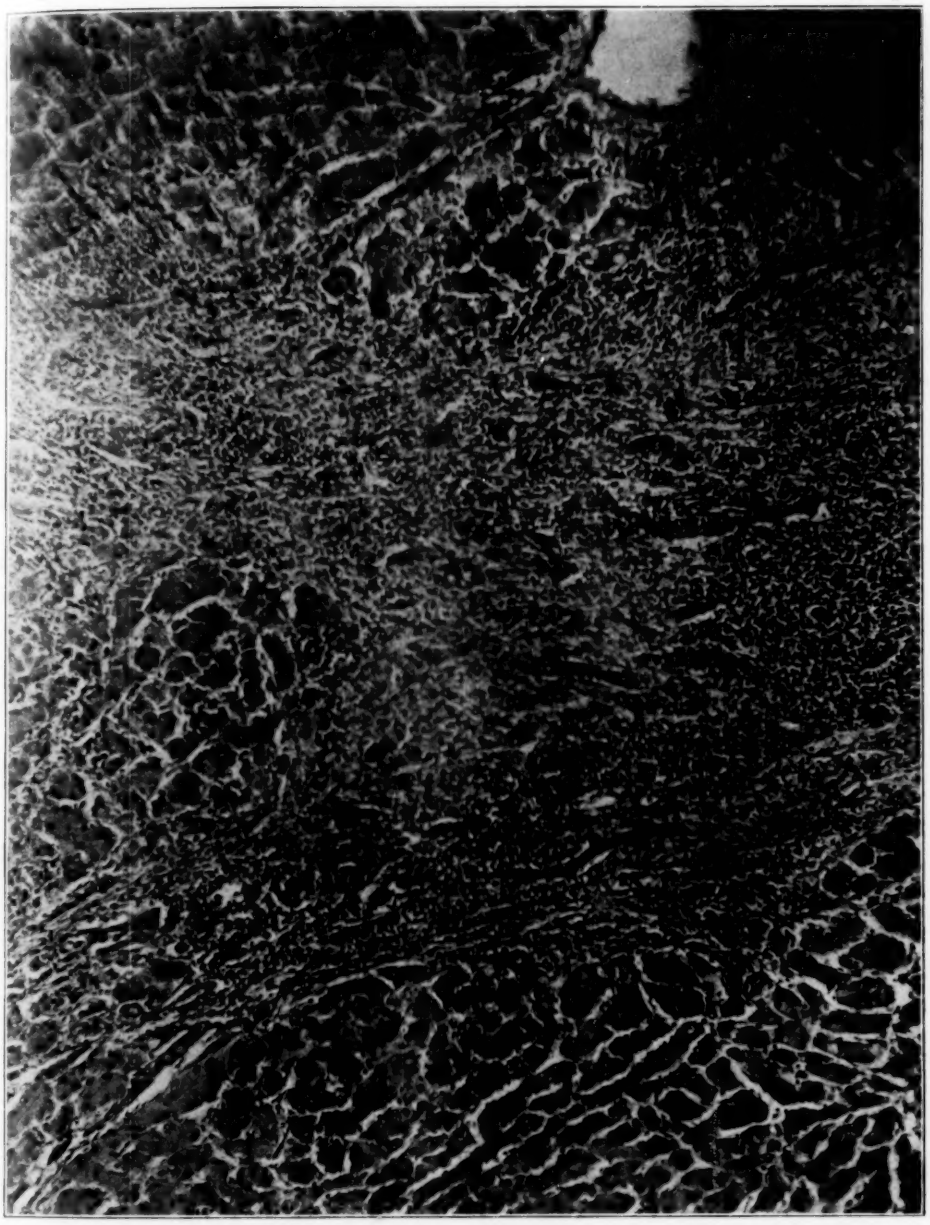
Date	Red Blood-Cells	Hemoglobin	White Blood Cells	Polymorphonuclears, per Cent	Lymphocytes, per Cent	Large Mononuclears, per Cent	Eosinophils, per Cent	Basophils, per Cent	Transitionals, per Cent
1/16/28	3,200,000	50	7,500	60	39	..	..	..	1
1/23/28	3,250,000	54	7,650	59	39	..	1	..	1
2/25/28	3,660,000	55	5,900	58	40	..	..	..	2
4/ 9/28	2,870,000	40	6,450	66	29	1	1	2	1

The roentgenogram of the chest showed considerable lung root and peribronchial thickening.

Because of the evidence of fairly well advanced hepatic cirrhosis, that is, spider angiomas, icterus, decreased liver function, probably ascites and slightly dilated hemorrhoidal and abdominal veins, splenectomy was not advised. The patient was empirically given roentgen exposure over the spleen in nine weekly treatments of 60 Angström units.

At the time of his second admission to the hospital, the child appeared more ill and had lost 3 pounds (1.4 Kg.). A definite abdominal fluid wave and a slight edema of the ankles were noted. He died at home on April 19, 1928, after a short period of fever and extreme prostration together with a severe infection of the nasal and upper respiratory tract. The family physician performed a necropsy and sent some tissue specimens to Dr. William Ophüls of the department of pathology at Stanford University Medical School. Dr. Ophüls noted these microscopic observations: "Sections of liver show large strands of cellular fibrous tissue in which there are many 'new bile ducts.' The remnants of liver tissue show a marked compensatory hypertrophy, little evidence of degeneration. The pancreas is poorly preserved, but otherwise normal. The kidney is normal." Unfortunately, I was unable to obtain the details of the gross postmortem examination.

1. Goodpasture, E. W.: Fibrinolysis in Chronic Hepatic Insufficiency, Bull. Johns Hopkins Hosp. **25**:330, 1914.



Liver tissue section from the case described. This shows a large strand of fibrous tissue, with round cell infiltration and new bile ducts, surrounded by portions of the hyperplastic nodules of liver cells.

COMMENT

Cirrhosis of the liver is defined as a thickening or proliferation of the elements that make up the stroma. It is not surprising that such a common type of disease reaction should be produced by more than one agent. Classifications of the types of this disease, at present, are based partly on a few of the probable causes and partly on the slightly varying pathologic pictures. Since the causes are, however, so poorly understood, it seems best to work with a type division based principally on pathologic changes as follows:

A. Primary

1. Atrophic (Laennec's, portal, nodular); showing periportal scarring with nodular hyperplasia of liver cells in place of normally arranged lobules
2. Hypertrophic (Hanot's, biliary); with markedly irregular diffuse proliferation of connective tissue invading diseased liver tissue

B. Secondary, resulting from

1. Chronic passive congestion (cardiac) with cyanotic atrophy and fibrosis
2. Chronic biliary infection and stasis (biliary); no deep invasion of liver tissue by the fibrosis
3. Pigmentation
4. Syphilis, and possibly tuberculosis and malaria

All the primary forms may be due to similar causes. It is now thought, but not proved, that hypertrophic cirrhosis is a more recent and more severe (subacute) inflammatory process alike in etiology with the atrophic type. Many of the reported cases of biliary cirrhoses have shown deep invasion of the liver tissue by the fibrosis, but these have not been proved to be due to infection. Many instances are recorded of cases of so-called typical Laennec's cirrhosis in which alcoholism has been excluded as an etiologic factor.

Children may develop any one of the foregoing listed types of cirrhosis. A good many of the children with atrophic cirrhosis have a definite history of alcohol ingestion. Jones,[2] in 1907, reported two cases and collected reports in the literature of seventy-two others probably due to alcohol. From Europe and Great Britain come most of the reports of the atrophic type. Rolleston[3] stated that among 16,100 necropsies at St. George's Hospital from 1865 to 1918 there were twelve cases of portal cirrhosis in persons under 21 years of age,

2. Jones, Ernest: Alcoholic Cirrhosis of the Liver in Children, Brit. J. Child. Dis. **4**:1, 1907.

3. Rolleston, Sir H., in Oxford Medicine, Oxford University Press, New York, 1921.

and that Woolley collected ninety cases in persons under 21 years, the average age being 11 years in both sexes. Lauré and Honorat [4] reported five cases, two of which were proved by necropsy. Hanau [5] reported four cases with three necropsies. There are a great many cases of so-called biliary infantile cirrhosis reported from India showing a distinct family incidence. The pathologic changes in these are similar to the original description of hypertrophic cirrhosis by Hanot. In the reports a sharp distinction cannot be drawn between these and the changes occasionally observed in infants and children in various parts of the world, presumably following biliary infection and stasis.

In America there are few reports of cirrhosis of infants and children. A considerable proportion of them were of the so-called biliary type, either primary hypertrophic or secondary to infection and stasis. Of the cases like the primary atrophic type, there were a good many with an alcoholic history. I have only been able to find, in an exhaustive search, reports of twelve proved cases of nonalcoholic atrophic cirrhosis from America.[6] The present case makes the thirteenth. I have also found ten cases of atrophic cirrhosis reported from America given with a history of the use of alcohol.[7] There were a few

4. Lauré, P., and Honorat, M.: Etude sur la cirrhose infantile, Rev. mens. d mal. de l'enf. **5**:97 and 159 (March and April) 1887.

5. Hanau, F.: Beitrag zur Kenntnis der hepato-lienalen Systemerkrankung, Monatschr. f. Kinderh. **29**:54 (Oct.) 1924.

6. Northrup, W. P.: Specimen presented before stated meeting of N. Y. Path. Soc., M. Rec. **23**:525, 1883. Peters, J. C.: Statement before stated meeting of N. Y. Path. Soc., M. Rec. **23**:526, 1883. Howard, R. P.: On Hepatic Cirrhosis in Children, Am. J. M. Sc. **94**:350, 1887. Pepper, W., in discussion on Howard's paper read before A. Am. Physicians, Wash., 1887. Brown, C. W. M.: Cirrhosis of the Liver in a Boy of 9 Years, Arch. Pediat. **10**:48 (Jan.) 1893. Edwards, W. A.: Cirrhosis of the Liver in Childhood, Arch. Pediat. **12**:481 (July) 1895. Abbe, Robert: Specimen presented at stated meeting of the N. Y. Surg. Soc., Ann. Surg. **22**:515, 1895. Fotheringham, J. T.: Cirrhosis of the Liver in the Young, Canada Lancet **36**:318, 1902-1903. Hamilton, W. F.: Cirrhosis of the Liver in Childhood, with Notes on Three Cases, Internat. Clin. **2**: 244, 1903.

7. Biggs, H. M.: Case of Alcoholic Cirrhosis of the Liver in a Boy, Aged 13, M. Rec. **38**:206, 1890. Abrahams, R.: A Case of Alcoholic Cirrhosis of the Liver in a Baby, Pediatrics **9**:186, 1900. Osler, W.: Two Cases of Cirrhosis of the Liver in Children, Bull. Johns Hopkins Hosp. **14**:322, 1903. Blakely, D. N.: A Case of Alcoholic Cirrhosis in a Boy of 4 Years, Boston M. & S. J. **162**: 245 (Feb. 24) 1910. Davis, G. R.: Cirrhosis in a Boy of Four Years, W. Virginia M. J. **7**:162, 1912-1913. Ely, Theodore: Two Cases of Cirrhosis of the Liver in Childhood, Boston M. & S. J. **170**:542 (April 2) 1914. Kay, M. B.: Case of Portal Cirrhosis in a Child, with Operation (Thalma-Morrison), J. Michigan M. Soc. **21**:244 (June) 1922. Elterich, T. J.: Alcoholic Cirrhosis in Child, Atlantic M. J. **30**:788 (Sept.) 1927. Griffith, J. P. C., and Mitchell, A. G.: The Diseases of Infants and Children, Philadelphia, W. B. Saunders Company, 1927, vol. 2, p. 221.

analyses of series of patients with cirrhosis which include occasional unproved or unclassified cases in childhood. Nodular cirrhosis has also been reported infrequently as probably due to syphilis. Some of these might have been included more correctly in the foregoing figures.

From the facts concerning the case here presented, it seems important to emphasize, for those treating diseases in children, the possibility of occurrence of atrophic cirrhosis in a child.. A negative history in regard to alcoholism does not rule out this possibility. A disturbance with fever, icterus and gastro-intestinal upset (a train of symptoms associated with the diagnosis of catarrhal jaundice), may occasionally lead to a later hepatic fibrosis through some toxic action on the liver. Many may err in making a less exact diagnosis of Banti's disease on seeing a child with such a splenic enlargement and blood picture as this boy showed. Weber [8] emphasized the intimate clinical connection between so-called Banti's disease and "idiopathic non-alcoholic progressive hepatic cirrhosis." He said that in the former the morbid process is located mainly in the spleen. The important point for the clinician is to consider well how far the liver changes have advanced before advising splenectomy in a case of possible Banti's disease.

The occurrence of large spider angiomas in a child should not be passed over lightly. It is not uncommon to see a few small or single changes of this type in children presumably following trauma to the skin. The larger ones, however, as pointed out by Gilbert and Herscher,[9] are often associated with hepatic insufficiency, and their occurrence should at least make one inquire further about liver function. It is interesting that in both the similar cases reported by Howard in 1887 there was a "nevoid group of blood vessels" on an eyelid, as was observed in this case.

Family incidence of cirrhosis in childhood has been emphasized by Bramwell,[10] Szanto,[11] Schuscik,[12] Gunn,[13] Poynton and Wyllie,[14] as

8. Weber, F. P.: Nature of Banti's Disease: Its Differentiation from Other Types of Splenomegaly and Its Relation to "Idiopathic" Nonalcoholic Progressive Hepatic Cirrhosis in Children and Young Persons, Brit. J. Child. Dis. **20**:78 (April-June) 1923.

9. Gilbert, A., and Herscher, M.: Des naevi artériels et capillaires dans les maladies du foie et des voies biliares, Compt. rend. Soc. de biol. **55**:167, 1903.

10. Bramwell, B.: Familial Cirrhosis of Liver: Four Cases of Acute Fatal Cirrhosis in the Same Family, Edinburgh M. J. **17**:90, 1916.

11. Szanto, J.: Familiär Auftretende Splenomegale Lebercirrhose, Monatschr. f. Kinderh. **36**:393, 1927.

12. Schuscik, O.: Ueber einen Fall von familiärer Kindlicher Leberzirrhose, Arch. f. Kinderh. **68**:144 (Aug.) 1920.

13. Gunn, F. D.: Familial Juvenile Cirrhosis of the Liver, Arch. Path. **1**:527 (April) 1926.

14. Poynton, F. J., and Wyllie, W. G.: Hepatic Cirrhosis in Children: Biliary Forms, Arch. Dis. Childhood **1**:1 (Feb.) 1926.

well as those reporting the Indian cases, but in this boy's large family there was no other history of similar disturbance. Moreover, this familial tendency seems to be observed in the hypertrophic types, showing marked fibrosis and deep invasion of the liver tissue, with the exception of the two cases of Howard.

It seems likely in the present cases that cirrhosis was a sequence of the earlier hepatic infection (so-called infectious jaundice). While such an outcome of what is commonly regarded in children as a comparatively mild disease without serious sequelae is exceptional, it is well to remember that it can occur. Possibly lesser degrees of permanent damage to the liver from catarrhal jaundice are by no means uncommon.

SUMMARY

1. The nature and occurrence of cirrhosis in childhood is discussed.

2. The thirteenth American case of nonalcoholic primary atrophic cirrhosis of the liver in a child is reported.

3. A warning is given concerning the easy confusion of primary cirrhosis with Banti's disease in relation to the question of splenectomy.

4. The onset of the disease with a disturbance like catarrhal jaundice, and the occurrence of large spider angiomas of the skin in association with cirrhosis are again emphasized.

FAMILIAL CONGENITAL SPASTIC DIPLEGIA

REPORT OF THREE CASES IN ONE FAMILY *

FLORENCE POWDERMAKER, M.D.
NEW YORK

Interest in the etiology of infantile spastic diplegia has been keen since its first description as a clinical entity by Little, and discussion of the possible factors has been carried on with interest and spirit. Little himself apparently considered, at first, that the same entity might be congenital or acquired, as he stated in his classic description that "you may meet with rare cases in which the whole of the muscles of the extremities . . . appear conjointly spastically affected . . . sometimes flexion predominates in the trunk, sometimes extension. Every form of contracture may present itself either as a congenital affection, or as the result of disease during infancy. A common accompaniment of (congenital or acquired) contractures, and particularly when at the same time muscles of the face are involved, is an impairment of the intellectual powers." [1] In a later publication,[2] however, he gave as the etiologic factors: prematurity, difficult labor and mechanical injuries to the head and neck during parturition, but stated "that asphyxia neonatorum through resulting injury to nervous centers, is the cause of the commonest contractions which originate at the moment of birth, namely, more or less generalized spastic rigidity. . . ." [3] He excluded gross lesions and gross injuries and pointed out the common association of diplegia with microcephaly. Only those cases of diplegia originating at birth are, strictly speaking, Little's disease. The term is widely used, however, in all cases of cerebral diplegia, the symptoms of which appear at birth or shortly thereafter without regard to the fact that they may have originated prenatally and regardless of any apparent etiologic factor. The relation is not clear between this syndome and the familial cases in which the symptoms may not appear until relatively late, without apparent cause, but often with a history of early developmental retardation.[4]

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* Submitted for publication, Aug. 26, 1929.

* From the Clinical Research Department, Letchworth Village, Thiells, New York.

1. Little, W. J.: On the Nature and Treatment of the Deformities of the Human Frame, London, Longman, Brown, Green & Longmans, 1853, p. 113.

2. Little, W. J.: On the Influence of Abnormal Parturition, Difficult Labors, Premature Birth, Asphyxia Neonatorum on Mental and Physical Condition of Children, Especially in Relation to Deformities, Tr. Obst. Soc. Lond. **3**:293, 1862.

3. Little (footnote 2, p. 300).

4. Oppenheim stated in his Textbook of Nervous Diseases (1911, vol. 1, p. 182), in a discussion of Little's disease, that "if we include the cases of hereditary stiffness of the limbs which at least are very closely related to the congenital form, we have to remember that the disease may occur even in adult age and may have a chronic progressive form."

Diplegia is used in this report to indicate a spastic paralysis involving the lower extremities more than the upper, in contradistinction to double hemiplegia in which the reverse is the rule.

In a review of the literature, Ford [5] discussed four theories of etiology besides that of asphyxia neonatorum: meningeal hemorrhage, arrested development due to prematurity, a degenerative process in utero and a congenitally defective development of the brain. Hemorrhage was claimed to be the etiologic factor by MacNutt,[6] and was widely accepted; though, as was later shown by Freud,[7] Collier [8] and others, it was based on the mistaken interpretation of the studies of three cases, and was not confirmed by the careful observations of others. In the main, however, emphasis has been placed on prematurity and birth factors, although Ford [5] found in the study of 200 cases that birth had been premature in 32 per cent and that difficult labor had occurred in only 15 per cent, and Collier [8] stated that 40 per cent of the cases reported were without any pathologic factor connected with birth. The notion of birth injury, however, as the causative factor, lingers. Adie,[9] in a symposium on Little's disease, did not apparently consider intra-uterine factors, since he stated that he "takes his stand on birth injuries in contrast to meningeal hemorrhage, as the most important etiological factor." Even though he stated that in many cases labor was normal, he made reference to the work of Schwartz who believed that injury frequently occurs under the presenting part of the head, due to differences in intra-uterine and atmospheric pressure. This factor, however, must operate in some degree in every birth.

There are also vigorous proponents of the hypothesis that spastic diplegia is a primary degenerative process of cerebral neurons. The theory was first advanced by Freud and defended by Collier, who is of the opinion that whatever may be the original cause of it and whether it occurs before or after birth, the typical pathologic condition is one of degeneration of the neurons, with atrophy and sclerosis. Other types of lesions have been described and confirmed by numerous workers, although it is generally conceded that the atrophic lobar sclerosis is most commonly found. One may find a brain that appears to show only slight developmental faults in the pyramidal tract, or one may find a gross developmental defect apparent in the simple fetal convolutions. It appears, therefore, from the pathologic observations that the condi-

5. Ford, F. R.; Crothers, B., and Putnam, M. C.: Birth Injuries of the Central Nervous System, Medicine Monographs, vol. 11, Baltimore, Williams & Wilkins Company, 1927, p. 23.

6. MacNutt, S. J.: Am. J. M. Sc. **89**:85, 1885.

7. Freud, S.: Die Infantile Cerebrallähmung, Vienna, Alfred Hölder, 1897.

8. Collier, J. S.: Pathogenesis of Cerebral Diplegia, Brain **47**:1 (Feb.) 1924.

9. Adie, W. J.: Spastic Paralysis, Brit. M. J. **2**:1208, 1926.

tion may be due either to deterioration or to an inhibition to development. This theory is also supported by the work of Ford. It may well be that the stage of development of the brain at the time of onset as well as the severity of the cause, whatever it may be, may determine the pathologic changes.

This, of course, does not answer the question of the primary causative factor. Syphilis, defective inheritance and maternal intoxication have been considered as etiologic factors. Undoubtedly cases of cerebral diplegia are found in conjunction with congenital syphilis, though in other cases it has undoubtedly been ruled out.

The three cases of familial spastic diplegia described are presented because of the rarity of familial cases and because the histories are unusually detailed and extraordinarily lacking in all those external factors that have been considered at one time or another as etiologic in this condition. They seem to confirm the theory of a prenatal factor. In the familial cases reported in the literature, many are associated with syphilis. In others, without any apparent cause, the onset in different members of the family may occur at various ages, as well as at birth. The question as to whether the latter cases belong in the same category as Little's disease was previously considered.

Stiefler [10] recently reported the occurrence of more than one case of congenital diplegia in siblings in three families. Two families were syphilitic, but the third, which had no record of syphilis, contained a pair of 7 month twins whose birth was difficult and who suffered from asphyxia neonatorum. The mother was an imbecile, but there were five older children apparently normal physically and mentally. Oppenheim also reported a case of diplegia in twins. In Stiefler's discussion of Freud's monograph, he described one family, in a total of fifty-three cases, in which two siblings apparently had congenital diplegia. He found in the literature the report of four other families, with a total of nine children, in which the weakness had been present from birth. Three of the seven births, for which there were histories, were normal. There was no mention of syphilis. Freud quoted from Feer [11] the cases of three children of the same mother; the first, born after difficult labor, was asphyxiated and diplegic from birth; the second had an easy birth and suffered from a severe diplegia from birth, and the third was well and strong at birth but had a progressive diplegia, which started when the child was 7 months old. Similarly, Krafft-Ebing [12] reported a case in which one sibling was diplegic at birth, another at 3 years of age and

10. Stiefler, G.: Littlesche Krankheit bei Geschwistern und bei Zwillingen, J. f. Psychol. u. Neurol. **37**:362, 1928.

11. Feer: Ueber angeborene spastiche Gleidestarre, Basle, Teubner, 1890.

12. Krafft-Ebing: Wien. klin. Wchnschr. **47**:681, 1892.

a third at 5 years; in the last two, the condition progressed slowly until the children were 10 years old, after which the condition remained stationary. Oppenheim, quoted by Freud,[7] reported a case of cerebral diplegia in a child of 10 years whose mother was similarly afflicted.

Newmark [13] reported cases in two families with incomplete family trees of three generations showing a marked familial tendency toward spasticity, with and without weakness. In one family, two children showed a weakness of the legs and a spastic gait with no disturbance of the hands and arms. A first cousin had a typical cerebral diplegia; the mother, aunt and three other children showed exaggerated reflexes but no weakness. The maternal grandmother had been feebleminded and deaf from childhood. In the other family, two children showed spasticity without weakness and the third a true spastic paralysis. The onset in all three occurred between the ages of 7 and 9 years. The histories in both families were negative for syphilis, but there was no serologic examination. That these conditions, however, are the same as the others discussed could not be affirmed, and only careful pathologic studies could solve the problem.

REPORT OF CASES

Family History.—The family history was known for three generations and the members were of intelligent, healthy Irish farmer stock. On the paternal side, the grandparents died of old age at 75 and had always been healthy. They had four boys and two girls, all living and well, married and having normal children. The maternal grandfather was living and well. The grandmother died in childbirth after having seven normal children and no miscarriages. They were all living and well, married and had normal children. There was no history of endocrine disturbances, syphilis, mental disease, epilepsy or mental defect.

The father was killed in a railroad accident. He had always been healthy and was not alcoholic. The mother was an unusually healthy woman, stable and intelligent. She was somewhat overweight, but not pathologically so. She reported never having been ill, and during her seven pregnancies was not even nauseated. All the labors were easy, except the first, and lasted for about two hours. All pregnancies were full term. There were no miscarriages. Nothing distinguished the pregnancies of the three patients from those of the others, who were healthy, fine-looking, well adjusted children at or above the average intelligence.

Siblings: A boy, aged 21, was born after a nineteen hour labor; it was a forceps delivery. He graduated from high school at 17 and later from business college.

A girl, aged 19, graduated from high school at 17. She was self-supporting.

There were also a boy (case 1), aged 17; a boy (case 2), aged 16; a boy, aged 14, who just graduated from the eighth grade; a boy (case 3), aged 12, and a boy, aged 10, who was in the sixth grade.

Case 1.—A boy, whose birth weight was 8 pounds (3.6 Kg.), was breast-fed until he was 1 year old. The child never seemed normal to the mother, as from birth there was some difficulty in swallowing, and development was delayed.

13. Newmark, L.: Contribution to the Study of the Family Form of Spastic Paraplegia, Am. J. M. Sc. **105**:432 (April) 1893.

Dentition did not begin until the age of 11 months. He sat up at 1 year, walked with difficulty and became clean in his habits at 4 years. He had bilateral otitis media at 2 years, lasting one month, and measles and chickenpox in infancy. He had whooping cough at 5, and several convulsions when about 15.

The patient was a thin, fairly well nourished boy. The head was microcephalic in contour but not in measurement (table). There was a marked elevation from the coronal suture to the upper border of the occiput. The skin was normal, moderately moist and showed a red line when streaked. The hands and feet were well proportioned. There was no body hair, except on the symphysis, where it showed masculine distribution. The pupils were equal and large, reacting, but not sustaining the reaction, to light and in accommodation. There was no strabismus or nystagmus. Hearing was apparently normal. The arch of the palate was low and broad. The tongue had a normal surface, but there was no control

Fig. 1 (case 1).—Illustrating the degree and type of deformity of the patient.

of it, and there was drooling. The teeth were regular and of normal shape. The thyroid was not palpable. The lymph glands were normal. The examination of the heart and lungs gave negative results. The pulse rate was 94, and the blood pressure, 128 systolic and 90 diastolic. The abdomen was normal. The genitalia were those of a normal adult.

The patient could walk alone. There was a tremor of the entire body when he was at all excited. There were fine to coarse tremor and slight athetoid movements of the hands. Coordination of the finger-to-nose movements was poor. There was no adiadokokinesis. The musculature of the face was normal, that of all extremities, spastic. There was left talipes equinus. Sphincter control was present.

The left and right biceps, triceps, ulnar and radius reflexes were increased. The right and left patellar and achilles reflexes were exaggerated. The pectoral reflexes, right and left side, were exaggerated. The jaw reflex was increased. The Chvostek sign was absent. The abdominal and scrotal reflexes were present.

The right Babinski sign was fanning; the left, suggestive. The right and left ankle reflexes and patellar clonus were inexhaustible. The right and left Oppenheim, Gordon, Schäffer and Shaddock reflexes were absent. The pharyngeal reflex was exaggerated.

CASE 2.—A boy, whose birth weight was 6½ pounds (2.9 Kg.), was never normal, according to the mother, as he had to be bottle-fed because he could not take the breast. He had always been nervous and easily frightened. He never walked and never talked. He had whooping cough and measles at 3 years. Paralysis was more marked after the whooping cough.

The patient was a thin, moderately well nourished boy, with a typical microcephalic head. The hair was normal in texture, the body hair being scant. The skin was dry and reacted to pressure with a red line. The fingers were long and tapering, and the toes were well proportioned. Retroflexion of the finger joints was marked. There was marked depression of the upper part of the sternum extending to the sixth rib. The eyes were normal except for eccentric pupils. The ear lobes were large. The arch of the palate was intermediate. The teeth were spaced, saw-edged and irregularly shaped. The thyroid was not palpable. He drooled almost constantly. The heart and lungs were normal. The

Fig. 2 (case 2).—Illustrating the degree and type of deformity of the patient.

pulse rate was 81. There was a slight mottling of the hands. The abdomen was normal and the genital development was preadolescent.

The patient could not stand but could pull himself up to a sitting position unaided and raise his head. Fine tremor of the body was almost constant, and there was a fine to coarse tremor of the fingers. He could move and take hold of objects with the left hand but not with the right. Both arms were flexed at the elbow. The right hand was markedly flexed at the wrist. The musculature of the left side of the face showed a slight weakness. He could not protrude the tongue. There was a marked contracture of all four extremities, with the legs in the scissors attitude. The muscles of the legs were more atrophic than those of the arms. Sphincter control was present.

The biceps and triceps reflexes were exaggerated; the ulnar, radius, patellar and achilles reflexes were increased. The abdominal reflexes were present and the scrotal were absent. The Babinski sign was absent. The right ankle clonus was exhaustive. Left ankle and right left patellar clonus was absent.

CASE 3.—A boy, whose birth weight was 6¾ pounds, was breast-fed. He also never appeared normal. There were frequent convulsions; he was restless and nervous and never walked or talked. He had measles and whooping cough during childhood.

The patient was a thin, fairly nourished child, with typical microcephalic head. He drooled constantly. The hair was normal, and there was no body

hair. There was marked retroflexion of the fingers. The hands and toes were well proportioned. The eyes were normal, except for slightly eccentric pupils. Hearing was apparently normal. The lobes were flaring. The arch of the palate was intermediate, and the teeth were regular. He had pyorrhea. The thyroid was not palpable. The lungs and heart were normal; the pulse rate was 81. There was cyanosis of the hands and feet. The abdomen was normal. Genital development was preadolescent.

The patient was unable to stand. He started at the slightest movement in his vicinity. There was a coarse tremor of the fingers. Coordination in the finger-to-nose test was good; he could not move the legs enough to test them. He could pull himself up and sit propped on his elbow, the arms being less affected than the legs. The tongue could not be protruded. The musculature of the face was normal, that of all extremities, spastic. The muscles of the legs were not as atrophic as those of the patient in case 2. The arms were kept flexed at the elbow and slightly at the wrist. There was slightly more strength in the right hand than in the left, and the left leg was more flexed than the right.

The right and left biceps, triceps, patellar and achilles reflexes were exaggerated. The pectoral reflexes were increased. The abdominal reflexes were present, the scrotal absent. The left and right Babinski signs were suggestive.

Fig. 3 (case 3).—Demonstrating the degree and type of deformity of the patient.

Right ankle clonus was exhaustible. Patellar reflex and left ankle clonus were absent. The Oppenheim reflex on the right and left was suggestive. The Gordon, Schäffer and Shaddock reflexes were absent. The jaw and pharyngeal reflexes were exaggerated.

Laboratory Observations.—Two Wassermann tests on the blood taken at intervals of six months on each of the three patients gave negative results; Wassermann reactions of the spinal fluid were negative, as were the colloidal gold curves. The cell counts were 7, 5 and 0, respectively. In case 1 the second spinal fluid examination two and three-fourth years later gave the same results. The sugar content of the fluid in case 1 was 56 and 59 mg., respectively.

Chemical examination of the blood in case 1 showed a calcium content of 11.4 and 11.8 mg.; sugar, 90.9 mg., and nonprotein nitrogen, 50 mg. per hundred cubic centimeters. Red cell counts in cases 1 and 3 were 5 million each, and in case 2, two counts at intervals of a month were 5,990,000 and 5,970,000. White counts were normal. The hemoglobin content was 75, 85 and 75 per cent, respectively. Urinalyses for all three patients gave negative results.

Basal metabolism tests were attempted in a further effort to find out whether the endocrine system was involved, but they were unsuccessful in cases 2 and 3 because of the tremor and the inability to keep the mouthpieces properly adjusted. The patient in case 1 had fourteen tests over a period of ten days. At first he

was frightened and did not cooperate, the results being + 47 and + 27. There was marked tremor. He gradually seemed to become accustomed to it, lay quietly, and the rate fell each time (+ 24, + 21, + 11, + 5). On the last six tests on three different days, satisfactory tracings were obtained. The average was — 19, the readings being — 24, — 13, — 18, — 24 and — 21.

Anthropometric measurements are given in the accompanying table.

Anthropometric Measurements

	Case 1	Case 2	Case 3
Age	17.5 years	16.8 years	12 years
Height	153 cm.		
Weight	40.9 Kg.		
Head, length (maximum)	17½ inches	16 inches	16½ inches
Head, breadth (maximum)	13 inches	11½ inches	11½ inches
Head, horizontal girth	20¼ inches	17½ inches	18¼ inches
Head, bizygomatic breadth	12 inches	10½ inches	10½ inches
Head, minimum frontal breadth	11 inches	10½ inches	10 inches

Mental Level.—All three patients had pleasant personalities; they tried to help themselves and to cooperate as far as they could. They smiled and laughed with a deep gurgling sound at the least attention paid them and were sufficiently alert to try to gain attention. Since they could not talk, many of the ordinary tests could not be carried out. Such nonlanguage tests in the Merrill-Palmer series were made as the limitations of their spasticity would permit.

In case 1 the patient solved simple problems by the random trial and error method on the Wallin Pegboards *A* and *B* and Seguin Formboard. Little or no reasoning ability was evident. Form and size perception were evidently absent and color perception was very poor, though he knew what the word "color" meant. He was eager and interested and obeyed simple commands. His imitative ability was his outstanding trait. His mental age was probably about 3 years.

In case 2, the patient apparently had no form or color perception or ability to solve the simple problems that the first patient could. He was interested in trying. Verbal commands were understood and obeyed at about the 18 month level. The selections from Merrill-Palmer gave a mental age of about 2 years. Imitation was a marked trait. He also showed some initiative, picking up the reflex hammer when the examiner was not looking and trying out the ulnar and radial reflexes, obviously pleased with himself and trying to show it off.

In case 3, the patient's comprehension was lower than in the other two, as there was a failure to understand any but the simplest verbal commands at about a 1 year level and no apparent comprehension of form or color. The patient was alert and tried, but his interest was fleeting.

COMMENT

It is to be noted in the cases described that all of those exogenous etiologic props often brought forward are absent. The cases, however, are clinically typical. Undoubtedly syphilis may produce a cerebral diplegia clinically similar to Little's disease, but it seems to be excluded from these as well as from many other cases. Trauma at birth accounts for such a small proportion of the cases that even if it is causative rather than coincident in these few, it leaves a large number of cases unex-

plained. Prematurity exists in more cases, but still is absent from too many to be the sole factor and cannot be the cause per se as more than 90 per cent of premature infants develop normally. It may well be, as Freud suggested, that the same underlying cause is at the basis of both the paralysis and the prematurity.

It seems probable, therefore, that in such cases as the three described, the cause must lie either in some unknown intra-uterine or constitutional condition existing during the pregnancy or in a germ plasm defect. If the former existed in these cases, there was no evidence in the health of the mother, and it would have to be a recurring condition, since four siblings, one born after and one between the last two cases, are normal. Nothing distinguished the different pregnancies, although it is conceivable that changes in the blood supply, for example, might bring about marked fetal changes with no evident signs in the mother.

On the other hand, an apparently reliable history has been obtained for three generations, and it is singularly free from any evidence of mental or physical defect. This would not, however, necessarily invalidate a theory of germ plasm defect, since it might be due to a recessive mendelian character. As is well known, such characters do not appear unless both parents possess them, and then the chances are only 1 in 4 of its appearing. It may be carried for generations by a family without appearing, as the possibility of its coming to the surface occurs only when members of two such families mate. The fact that three of seven children are afflicted also does not necessarily nullify the theory, as the 1 : 4 ratio is apparent only when a large number of cases is included. The same theory has been advanced by Herrman [14] as an explanation for the similarly isolated occurrences of mongolism with the occasional appearance of children with familial cases along with normal siblings.[15] Unfortunately, one can do no more than to suggest this as a possibility. In the nature of things, no direct proof would be possible, and its final acceptance would depend on the disproving of all other theories—an equally difficult task.

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14. Herrman, Charles: Mongolian Imbecility as an Anthropologic Problem, Arch. Pediat. **42**:523 (Aug.) 1925.

15. Herrman, Charles: Etiology of Mongolian Idiocy, Arch. Pediat. **34**:494 (July) 1917.

Case Reports

HEMOLYTIC STREPTOCOCCIC SEPTICEMIA

REPORT OF A CASE WITH RECOVERY IN AN INFANT, AND A REVIEW OF FORTY-THREE CASES OF GENERAL SEPSIS *

CHARLES S. ROLLER, M.D.
LOS ANGELES

Septicemias caused by the streptococcus are among the most frequently encountered, as well as the most dreaded, of all general infections. In the greater percentage of cases, there is a fatal termination. Cooke [1] noted: "All hemolytic streptococcic septicemias, with only occasional exceptions are characterized by being terminal, and are accompanied by an extremely severe toxemia." He tabulated the incidence of septicemia with positive blood culture that he observed at the St. Louis Children's Hospital, and noted that there were forty-eight cases of hemolytic streptococcic septicemia out of a total of 104 cases. This shows the great frequency of this particular strain of organism in the etiology of septicemia in infants and children. Again, he stated that in a group of sixty patients with streptococcic septicemia, fifty-one were due to hemolytic and nine to nonhemolytic strains of the organism. In only one instance in this series did recovery follow the isolation of the streptococcus from the blood stream. This shows a mortality of 98.2 per cent.

Bean [2] reported fifty-eight cases of general sepsis. Of these, fifty-four were caused by the streptococcus, with a mortality of 83.9 per cent.

Pfaundler and Schlossman [3] said, "The prognosis is very serious. The more acute the course of the disease and the younger the infant, the more unfavorable the outlook."

Holt and Howland [4] stated, "Pyogenic infections in the newborn, even in their mildest form are serious, and in their most severe forms, almost always fatal."

Feer,[5] von Reuss [6] and many other authorities made, in substance, the same statements.

* Submitted for publication, June 24, 1929.

* From the Children's Hospital.

1. Cooke, Jean V.: Septicaemia, in Abt: Pediatrics, New Haven, Conn., Yale University Press, 1923, vol. 6, p. 516.

2. Bean, H. C.: Report of Fifty-Eight Cases of Septicaemia, Northwest Med. **25**:306 (June) 1926.

3. Pfaundler, M., and Schlossman, A.: Diseases of Children, ed. 2, Philadelphia, J. B. Lippincott Company, vol. 2, p. 71.

4. Holt, L. E., and Howland, John: Diseases of Infancy and Childhood, ed. 8, New York, D. Appleton & Company, 1925, p. 85.

5. Feer, E.: Pediatrics, first English ed., p. 147.

6. Von Ruess, August Ritter: Diseases of the Newborn, ed. 1, p. 540.

Since 1921, in a series of forty-three cases of general sepsis observed at the Children's Hospital, Los Angeles, ten have been proved by blood culture during the life of the patient to have been caused by the streptococcus. Five more cases were found by the pathologist to be streptococcic in origin by postmortem blood culture. All these patients died except the one whose case is reported in this paper. In the complete series of forty-three cases, a total of forty patients died. This gives a mortality of 93.1 per cent for the whole series, and of 93.4 per cent for the streptococcic cases. All methods of treatment used in this series met with universally poor results.

The literature abounds with articles on septicemia in infancy, but recoveries in proved cases are of sufficient interest to justify a report. In the case reported, recovery was not expected because the infant was already in an extremely debilitated and toxic condition before the onset of the septicemia.

REPORT OF CASE

History.—Robert F., aged 16 months, of American parentage, was admitted to the Children's Hospital on Jan. 18, 1929. The family history was negative. Development was entirely normal. The previous history was negative except that he had had measles at 10 months of age.

The present illness started about two weeks before admission, with a cold and fever. Shortly after this the mother noted that the glands of the right side of the neck were somewhat enlarged and at about the same time, there began to be a discharge from the right ear. A few days later, a tender enlargement behind the right ear was observed. The condition became gradually worse. The temperature ranged between 102 and 104 F. There was no cough, vomiting or diarrhea. The appetite had been poor since the beginning of the illness.

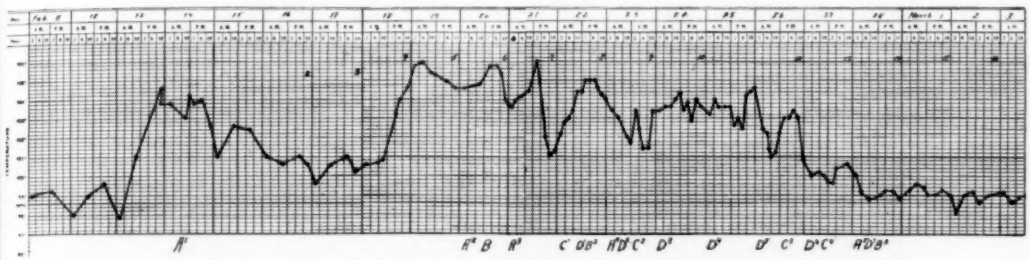
Physical Examination.—On admission the child appeared to be of the stated age, and looked acutely ill; he was extremely toxic and weak. There was a definite purulent discharge from the canal of the right ear, the right membrana tympani showing a posterior perforation. The right mastoid process was markedly swollen, edematous and tender. The right auricle was tipped forward by the posterior swelling. Except for the observation of a slightly injected throat and slight cervical adenopathy, nothing of importance was found on physical examination.

The urine was normal except for a one plus reaction to the acetone test. The red blood cells numbered 3,890,000; the white blood cells, 16,200; polymorphonuclears, 59 per cent; lymphocytes, 40 per cent, and eosinophils 1 per cent. Two hundred cells were counted. The hemoglobin was 50 per cent by the Dare method.

Operation and Course.—A right mastoidectomy was performed on the day of admission. Cultures from the pus liberated at operation subsequently revealed a gram-positive streptococcus in pure culture. The temperature came down the next day, and in three days was normal. The patient ran the usual postoperative course, except that recovery was rather slow. On the seventeenth postoperative day, he developed an otitis media on the left side. Myringotomy was promptly done. All local treatment, however, was found ineffectual, and on the ninth day after the development of otitis on the left side, it was found necessary to perform a mastoidectomy on that side. Pus cultured from this area contained the same

gram-positive streptococcus in pure culture. The operation was followed by an immediate drop in temperature and by general improvement, until on the fourth postoperative day the temperature suddenly rose to 106 F., and remained very high despite the usual treatment. At this time, the right mastoid was practically healed.

Lateral sinus thrombosis, septicemia, epidural abscess or meningitis were thought to be the most likely causes of the hyperpyrexia. There were no signs, however, of epidural or meningeal infection. The spinal fluid was normal, and there was no definite evidence that the lateral sinus was beginning to thrombose. The lungs were carefully examined daily, and at no time was there a suggestion of bronchitis, much less of pneumonia. There was no infection of the urinary tract. A blood culture was taken on February 20. Following this, the left lateral sinus was exposed and opened. There was free bleeding. The endothelium of the sinus lining was normal in appearance, and there was no evidence of thrombosis or of epidural infection in the locality. The child's condition did not permit exposure of the jugular bulb. Bleeding was easily and quickly controlled by iodoform packs left in situ. As the hemoglobin content was only 30 per cent (Dare), an intravenous transfusion of 180 cc. of whole blood was given



Temperature chart. A^1 indicates when a left mastoidectomy was performed; A^2, exposure and opening of the left lateral sinus; A^3, A^4 and A^5, intravenous transfusions of whole blood; $B,^1$ a positive blood culture; B^2 and $B,^3$ a negative blood culture; C^1, C^2 C^3 and C^4, the administration of polyvalent antistreptococcic serum intramuscularly and intravenously or both; D^1, D^2, D^3, D^4, D^5, D^6 and D^7, hypodermoclysis of 500 cc. of physiologic solution of sodium chloride.

on the same day. On February 22, the culture taken from the blood stream on February 20 showed a gram-positive streptococcus in pure culture which definitely hemolized blood agar. Accordingly, the child was given 20 cc. of polyvalent antistreptococcic serum (Lilly), 10 cc. in each buttock intramuscularly. Five hundred cubic centimeters of physiologic solution of sodium chloride was being given daily in divided doses subcutaneously; retention enemas of 5 per cent dextrose and 2 per cent sodium bicarbonate were also given, 3 ounces (89 cc.) every three hours. There was no vomiting at any time and the child was gavaged twice daily, milk and water being given; this was necessary for only a few days. The lips and the nailbeds were cyanotic; the temperature was persistently very high; the pulse was very rapid, weak and irregular, and the child was stuporous and could not be aroused from February 20 to 23, inclusive. Caffeine sodium benzoate, alternated with a digitalis preparation in suitable dosage, was given every two hours as a cardiac and circulatory stimulant.

On February 23, a blood culture was taken. This was followed by an intravenous transfusion of 175 cc. of whole blood; into the same vein was introduced

10 cc. of the antistreptococcic serum. Ten more cubic centimeters of serum was administered intramuscularly before the patient left the operating room.

On February 24, a slight improvement was noted in the morning. The infant was voluntarily taking some fluids by mouth. The temperature was down to a maximum of 103 F., and the pulse rate was better. All general systemic measures were continued.

On February 26, the child was slightly better. The blood culture of February 23 was negative for seventy-two hours. Ten cubic centimeters of serum was administered intramuscularly.

On February 27, the temperature dropped to almost normal for the first time in nine days, and there was definite improvement in the clinical condition of the infant. Ten cubic centimeters of serum was given intramuscularly.

On February 28, the child was taking both fluids and nourishment fairly well by mouth. The retention enemas were discontinued. The child had developed an irritative diarrhea on the last day that the enema was employed, no doubt owing to the continued presence of dextrose in the lower bowel. This promptly cleared up when the enema was discontinued.

On March 1, a third blood culture was taken and was followed by an intravenous transfusion of 150 cc. of whole blood.

By March 2, the infant was taking nourishment and fluids well by mouth. The improvement was striking. The daily hypodermoclysis was discontinued. The packs were removed from the left lateral sinus on the fifth postoperative day, with no bleeding. The hemoglobin was 51 per cent on March 6 and 70 per cent (Dare) on April 2. The child was discharged from the hospital on April 8, with only slight drainage from the left mastoidectomy wound. The gain in weight and general nutrition during the last few weeks in the hospital was marked.

COMMENT

The infection in this case may have entered the blood stream through the left lateral sinus or the left jugular bulb, or it may have gained entry through any of the open vessels in the recent mastoidectomy wound. Possibly it may have entered through the almost completely healed right mastoid or middle ear.

The diagnosis was established in this case by: (1) the temperature chart, (2) the positive blood culture and (3) the satisfactory elimination of other possible complications. A thrombotic change, however, may have been present in the jugular bulb. If this was the case, recovery occurred without further operative intervention or further complications.

There was no evidence of acute damage to the kidneys, a frequent complication of septicemia.

It will be remembered that both mastoid cultures taken at operation produced streptococcus in pure culture. It was, without much doubt, the same organism that was recovered from the blood in the culture of February 20. This culture was taken when the temperature was almost 106 F. Most observers agree that cultures taken while the temperature is 104 F. or above, in children, are much more likely to be positive than cultures taken during a remission, as it is probable that the high points of temperature in septicemia coincide with showers of organisms into

the blood stream. The other two cultures taken in this case remained negative after ten days' incubation.

The reproduced temperature chart shows the sudden rise of the temperature from normal to nearly 105 F. on February 13, and the gradual return to almost normal limits on the third day after the left mastoidectomy. Also it demonstrates graphically the sudden rise to 106 F. on the fourth and fifth postoperative days, and the nine days of high septic temperature alluded to in the report.

Several years ago, repeated blood transfusions seem to have been employed more commonly than recently as a treatment of choice in septicemia. I think that there is a definite tendency, however, to use this method now as a part of the treatment in every case of general sepsis. Theoretically this treatment would be more effective if the exsanguination method of transfusion, as recommended by some, was used whenever practicable. In any event, the universally high mortality with all methods of treatment indicates that no effective means of dealing with this condition has as yet been formulated. Some authorities give great credit to various dyes used intravenously; yet there have been recorded numbers of necropsies on patients dying with septicemia following mercurochrome therapy who have shown indisputable pathologic evidence of acute mercurial poisoning in the kidneys and gastro-intestinal tract. Neutral acriflavine and gentian violet are at least safer dyes to use intravenously. The use of stock serums and autogenous vaccines has likewise met with apparent success in a small percentage of cases. In the case reported, the dosage of serum was large; in fact, it could almost be called massive for an infant of this size and weight. Large doses of salicylates or of sodium cacodylate given by some have had beneficial effects in comparatively few cases. A series of patients treated with blood transfusions alone apparently show no better results, as a whole, than do those treated by other methods. The transfusions in this case were made with whole blood and were given slowly; the amounts were as large as could be given with safety. It is felt that a mistake was made in not giving the infant one or more transfusions after the first mastoidectomy to reduce the secondary anemia and to improve the general condition.

SUMMARY

1. It is conceded by all authorities on the subject that the mortality rate in general sepsis, and in streptococcic septicemia in particular, still remains extremely high.

2. A case of acute hemolytic streptococcic septicemia following a mastoidectomy is reported, in which blood transfusions, antistreptococcic serum and intensive supportive measures were used, with complete recovery.

3. There is no effective method of treating patients with general sepsis, but it is important to remember that no matter what methods are used, general supportive measures should be employed to the utmost extent.

4. Repeated intravenous transfusions of whole blood could well be considered part of the general supportive measures to be employed in all cases.

Progress in Pediatrics

THE AGE, SEX AND SEASONAL INCIDENCE OF CERTAIN DISEASES IN CHILDREN *

FREDERICK F. TISDALL, M.D.

ALAN BROWN, M.D.

AND

ARTHUR D. KELLY, M.D.

TORONTO, CANADA

A knowledge of the age, sex and seasonal incidence of many diseases of childhood is of considerable diagnostic value. We have been unable to find in the literature any recent statistics on all three aspects of the subject. Accordingly, the records of nearly 2,500 patients from birth to 13 years of age who were admitted to the Hospital for Sick Children during the past five years and about 5,000 records obtained from the Toronto Department of Public Health have been examined. The results are tabulated in tables 1 to 5. We fully realize in regard to the hospital records that certain of the diseases considered may be encountered in private practice at slightly different age limits. For example, the youngest patient admitted to the hospital with asthma was 1 year of age, while in private practice we have seen mild cases in children from 4 to 5 months of age. Nevertheless, we feel that the results here recorded are of definite practical value.

A brief summary of the points of interest are given under the heading of each disease, and the results are discussed under the heading of comment.

TYPES OF DISEASE

Endocarditis.—The records of 351 cases were examined. The youngest patient was 2½ years of age; four patients were seen at 3 years of age, two at 3½ and ten at 4 years. The disease was then encountered with approximately the same frequency each year in patients from 5 to 13 years of age. Forty-three per cent of the patients were males.

Rheumatic Fever.—The records of 108 cases were examined. The youngest patient was 2 years of age; two patients were seen at 3 years. From 4 to 13 years of age the disease was encountered each year with approximately the same frequency. Sixty per cent of the patients were males. No marked seasonal incidence occurred, although the greatest number of cases were seen in July (18 per cent).

* Submitted for publication, Oct. 25, 1929.

* From the Hospital for Sick Children.

Chorea.—The records of 188 cases were examined. The disease was encountered infrequently in patients less than 5 years of age, nine persons in all being seen under this age limit. The youngest patient was 3 years of age. The disease was encountered with approximately the same frequency each year after the age of 7 years. Thirty-nine per cent of the patients were males.

Scurvy.—The records of forty-eight cases of scurvy were examined. Thirty-three cases or almost 70 per cent occurred in infants from 6 to 12 months of age. This corresponds closely with our records for the preceding five years during which time 73 per cent of the patients were from 6 to 12 months of age.[1] In the present series almost 20 per cent of the cases occurred in patients 9 months of age. The youngest patient was 5 months, while at the other extreme there were only two patients over 2 years of age. Fifty per cent of the cases occurred during the four months of September, October, November and December.

Tetany.—The records of eighty-nine cases of tetany were examined. In the present series the youngest patient with tetany was 8 weeks old, although in a previous series two cases were encountered in which the patients were 7 weeks of age.[1] There were sixty-eight cases, or 76 per cent of the total, in which the patients were from 4 to 12 months of age. Only one patient, 22 months old, was encountered over 18 months of age. Sixty-eight per cent of the patients were males. Seventy-two patients, or 80 per cent of the total, were seen during February, March, April and May, while no less than one third of all the patients were seen during the month of March alone.

Intussusception.—The records of ninety-six cases were examined. The youngest patient was 2 months of age. There were sixty-eight cases, or 70 per cent of the total, in which the patients were from 4 to 10 months of age. The oldest patient was 7 years of age. Sixty-four per cent of the cases occurred during the six months from May to October.

Hemorrhagic Disease of the New-Born Infant.—The records of seventy-seven cases were examined. Three patients had hemorrhage at birth, while in ten patients the onset of the bleeding occurred during the first twenty-four hours. Forty-one patients, or 53 per cent of the total, started to bleed during the second and third days of life. The maximum age at onset was 10 days. Thirty-six cases, or 50 per cent of the total, were seen during February, March and April.

Pyloric Stenosis.—The records of 100 cases were examined. In eleven cases the patients vomited from the time of birth. This figure is probably higher than is actually the case because of the difficulty in

1. Tisdall, F. F.: Canad. M. A. J. **13**:346, 1923.

obtaining an accurate history of the time of onset in those patients in whom the vomiting started during the first few days of life. The most frequent time of onset was during the second and third weeks of life, although in one third of the cases the onset was not until after the third week. The maximum age at onset was 70 days. Eighty-two per cent of the patients were males. Forty-nine per cent of the cases occurred during the months of June, July, August and September.

Purpura.—The records of twenty-eight cases were examined. The patients varied in age from 1 month to 12 years. The disease occurred with slightly greater frequency during the winter months than during the summer months.

Erysipelas.—The records of 204 cases were examined. Eleven patients were less than 2 weeks of age, the youngest being 3 days old. Seventy-five per cent of the patients were 2 years of age or less. Sixty-six per cent of the cases were encountered during the first six months of the year.

Pyelitis.—The records of 131 cases were examined. The youngest patient was 9 days of age. Four patients were encountered at 3 weeks of age. During the first two years of life ninety-four patients, or 71 per cent, were seen. Cases occurred each year up to the age of 13 years, the maximum age observed. Eighty-one per cent of the patients were females. Forty-four per cent of the cases occurred during June, July, August and September.

Acrodynia.—The records of twenty-one cases were examined. The youngest patient was 8 months of age and the oldest 23 months. No less than five patients were seen at 8 months of age, although none was encountered before this age. Eleven patients, or 52 per cent of the total, were 8, 9 or 10 months of age.

Primary Peritonitis.—The records of thirty-two cases were examined. The youngest patient was 1 year of age. Twenty patients, or 62 per cent of the total, were under 6 years of age. The oldest was 10 years of age. Seventy-five per cent of the patients were females. Seventy-eight per cent of the cases occurred during the six months from January to June.

Appendicitis.—For purposes of comparison with the cases of primary peritonitis the records of 350 patients with acute appendicitis were examined, from the standpoint of the seasonal incidence. The results are given in table 5. Of 108 patients the youngest was 11 months of age. Only 19 per cent were under 6 years of age.

Typhoid.—The records of eighteen cases were examined. Three patients were under 5 years of age, the youngest being 23 months old. Fifty-six per cent of the patients were females. Five patients were

seen during the months of September. No patients were seen during January, February and March.

Retropharyngeal Abscess.—The records of seventy-two cases were examined. Thirty-three patients, or 45 per cent, were under 1 year of age; 38 per cent were seen during the second year of life and 17 per cent at a later period. The oldest patient was 13 years of age. Almost 50 per cent of the cases were seen during the three winter months, January, February and March.

Nephritis.—The records of 109 cases were examined. Twenty-seven patients, or almost 25 per cent, were 2 years of age or less. The youngest patient was 2 weeks old. Sixty-five per cent of the cases occurred during the six months from December to May.

Diabetes Mellitus.—The records of eighty-three cases were examined. The youngest patient was 22 months of age. Seven patients were encountered at the age of 2 years, and from four to nine patients were seen for each year thereafter.

Eczema.—The records of eighty-three cases were examined. Only eight patients were more than 2 years of age, the oldest being 5 years. The youngest patient was 3 weeks old. Almost 50 per cent of the patients were from 4 to 10 months of age. The disease occurred more frequently during March than any other month.

Asthma.—The records of forty cases were examined. Only three patients were less than 2 years of age, one 12 months, one 13 months and one 15 months. The disease was then encountered with approximately the same frequency in patients from 2 to 13 years of age. Sixty-five per cent of the cases were observed during the months of July, August, September, October and November.

Anterior Poliomyelitis.—The records of 109 cases were examined. No less than ten patients were 12 months of age or less, the youngest being 2 months of age. Sixty-four patients, or 58 per cent, were less than 5 years of age. Seventy-two per cent of the cases were encountered during August, September and October.

The records for the seasonal incidence of chickenpox, scarlet fever, measles and whooping cough were obtained from the Toronto Department of Public Health. Chickenpox was encountered most frequently during November, December and January and least frequently during August and September. Scarlet fever was observed most frequently during January, February and March and least frequently during July, August and September; measles most frequently during March, April, May and June and least frequently during August and September, while whooping cough was encountered with almost equal frequency each month from January to September. Whooping cough, however, had

its highest incidence during July. It was encountered with the least frequency during December.

COMMENT

Age Incidence.—A survey of the results here reported demonstrates conclusively that a knowledge of the age incidence of many of the diseases considered is of definite value to the practicing physician. Of 351 cases of endocarditis only seven, or 2 per cent, were in patients less than 4 years of age. The youngest patient was 2½ years old. The differential diagnosis between congenital and functional murmurs, on the one hand, and acquired murmurs, on the other, is thus greatly simplified in patients under 2½ years of age. On account of the close association of chorea and rheumatic fever with endocarditis, it is not surprising that these diseases also occur infrequently in patients less than 4 years of age. The youngest patient with rheumatic fever was 2 years old, and two were seen at 3 years of age, while only two patients with chorea were seen who were less than 4 years of age.

Many patients with scurvy are sent to the hospital with a mistaken diagnosis of rheumatic arthritis due to the pain and swelling at the ends of the long bones. Almost 70 per cent of the forty-eight infants with scurvy were from 6 to 12 months of age, and only two were more than 2 years of age. Of 108 patients with rheumatic fever only one was less than 3 years of age; so it is evident that the question of a differential diagnosis of these two diseases need hardly ever be considered. The youngest patient with scurvy was 5 months of age, and so one could infer that it is not essential to add the antiscorbutic vitamin to the diet of infants before the fourth or fifth month.

The age incidence for tetany is of considerable interest in view of its close association with rickets. The earliest authentic case of rickets occurred in an infant 34 days of age.[2] In the present series the youngest patient with tetany was 8 weeks old. Over 75 per cent of the patients were from 4 to 12 months of age.

The age incidence in intussusception approximates that of tetany in that 79 per cent of the patients with intussusception also were from 4 to 12 months of age. However, seven patients with intussusception were more than 2 years of age, while in the cases of tetany all the patients were less than 2 years of age.

The value of the knowledge of the age incidence is further demonstrated by the figures for the other diseases considered. In hemorrhagic disease of the new-born infants, the latest time of onset was after the tenth day. This is in agreement with most authorities who state that the disease never occurs after the twelfth day. Over 50 per cent of our

2. Dunham, E. C.: Rickets in Infants of Thirty-Four Days, Am. J. Dis. Child. **26**:155 (Aug.) 1923.

patients started to bleed on the second and third days of life. In regard to pyloric stenosis, vomiting from birth was comparatively rare, and the onset in the majority of patients occurred during the second and third weeks of life. Although the maximum age of onset in our series was seventy days, Davison [3] reported the case of a patient in whom vomiting did not start until the age of 8 months.

Acrodynia has been encountered in patients other than infants by many authors such as Weston [4] who had one patient 5 years of age, La Page [5] who had one 7 years of age and White [6] who found the disease even in adults. Although the number of patients with acrodynia in the present series is small, twenty-one in all, it is rather striking that the age of the patients varied only from 8 to 23 months.

TABLE 1.—*Age Incidence of Disease*

	Months														Years											
Disease	0 to 1	1	2	3	4	5	6	7	8	9	10	11	12	13 to 17	18 to 23	2	3	4	5	6	7	8	9	10	11	12	13
Scurvy	0	0	0	0	0	1	2	5	6	9	4	3	4	8	4	2	0	0	0	0	0	0	0	0	0	0	0
Tetany	0	0	1	4	7	3	17	10	12	9	4	5	1	15	1	0	0	0	0	0	0	0	0	0	0	0	0
Intussusception	0	0	1	3	7	13	13	10	13	5	8	3	4	6	3	5	3	1	0	0	1	0	0	0	0	0	0
Acrodynia	0	0	0	0	0	0	0	0	5	2	4	2	0	7	1	0	0	0	0	0	0	0	0	0	0	0	0
Diabetes	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	7	9	8	9	6	7	8	6	5	7	4	6
Nephritis	3	1	0	1	0	1	0	1	0	1	0	1	2	3	7	8	12	10	10	5	7	11	8	4	4	5	4
Purpura	0	1	1	0	0	0	1	1	0	0	0	0	1	0	1	2	1	2	1	2	3	1	1	2	3	2	1	0
Erysipelas	21	13	17	8	9	7	7	3	7	6	6	2	11	10	10	14	5	12	5	3	1	6	4	3	4	7	3
Anterior poliomyelitis	0	0	2	0	1	0	1	0	0	2	0	1	3	0	7	18	11	18	7	7	7	5	6	4	7	2	0
Eczema	1	7	4	3	8	5	11	4	3	5	4	1	1	9	6	6	2	1	2	0	0	0	0	0	0	0	0
Asthma	0	0	0	0	0	0	0	0	0	0	0	0	1	2	0	3	2	1	5	3	3	5	3	4	1	2	6
Retropharyngeal abscess	0	1	1	1	4	1	6	0	3	6	5	5	5	13	9	3	2	4	2	0	0	0	0	0	0	0	1
Pyelitis	5	5	1	2	5	7	9	5	4	3	8	9	5	13	5	8	8	4	5	3	2	4	1	1	2	0	5
Primary peritonitis	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	5	4	3	6	3	1	5	2	1	0	0	0
Acute appendicitis	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	3	1	9	5	5	5	13	7	18	10	20	9
Typhoid	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	1	1	2	1	2	2	2	1	3
Endocarditis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	6	14	30	28	40	46	35	45	25	44	37
Rheumatic fever	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	7	8	8	14	7	10	15	8	16	8
Chorea	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	5	12	13	24	18	25	20	24	21	22

Many authorities state that retropharyngeal abscess is encountered infrequently after the first year. In our series, only 45 per cent of the patients were less than 1 year of age, and 17 per cent were more than 2 years. The oldest patient was 13 years.

It is of interest to note that nephritis was encountered in patients only 2 weeks of age and pyelitis in patients 9 days of age. Both pyelitis and diabetes have been found in new-born infants [7] although in our series the youngest patient with diabetes was 22 months old. We found many cases of erysipelas in new-born infants. Asthma (severe hospital

3. Davison, W. C.: Bull. Johns Hopkins Hosp. **37**:75, 1925.

4. Weston, W.: Arch. Pediat. **37**:513, 1920.

5. La Page, C. P.: Lancet **1**:176, 1926.

6. White, C. J.: Acrodynia in Adults, J. A. M. A. **87**:1092 (Oct. 2) 1926.

7. Graham, R. H.: Am. J. M. Sc. **170**:401, 1925. Banting, F. G.: Personal communication.

cases) in contradistinction to eczema, with which it is closely associated, was rarely encountered in patients less than 2 years of age, while eczema, on the other hand, was rarely seen in the hospital in patients more than 2 years of age.

Anterior poliomyelitis was encountered more frequently in patients less than 5 years of age than in those more than 5 years. In a previous paper,[1] we reported a case of typhoid fever in a boy 5 months of age. A positive Widal test and blood culture made the diagnosis unquestionable. In the present series, the youngest patient was 23 months of age. The age incidence in measles has not been considered in the present

TABLE 2.—*Sex of Living Infants Born in Toronto from 1923 to 1927*

Year	Total Number	Males, per Cent	Females, per Cent
1923	13,119	52.0	48.0
1924	12,877	50.6	49.4
1925	12,456	51.6	48.4
1926	11,877	50.3	49.7
1927	12,340	52.5	47.5

TABLE 3.—*Sex Incidence of Disease*

Disease	Total Number	Males, per Cent	Females, per Cent
Scurvy	48	58	42
Intussusception	96	61	39
Purpura	28	57	43
Acute appendicitis	108	63	37
Retropharyngeal abscess	72	61	39
Nephritis	100	60	40
Diabetes	83	60	40
Anterior poliomyelitis	109	57	43
Epilepsy	125	60	40
Rheumatic fever	108	60	40
Scarlet fever	181	59	41
Eczema	83	63	37
Bronchopneumonia	207	58	42
Asthma	40	55	45
Hemorrhagic disease of new-born infant	77	55	45
Erysipelas	204	53	47
Acrodynia	21	52	48

series, because in a previous paper [1] we reported 1,031 cases in which only six patients were less than 6 months of age and only one less than 4 months of age.

Sex Incidence.—In table 2 is given the sex incidence year by year of the living infants born in Toronto from 1923 to 1927. The percentage of males is slightly greater than that of females. When we examine the sex of the patients admitted with the various diseases recorded in table 3, we find that the males constitute approximately 60 per cent of the total with few exceptions, instead of the expected 50 to 52 per cent. The figures are singularly constant and confirm the popular impression that male children are more prone to contract various diseases.

Only four of the diseases considered here occur predominantly in one or the other sex (table 4). In the cases of pyloric stenosis, 82

per cent of the patients were males. In tetany, male infants accounted for 68 per cent of the total. Bakwin and Bakwin [8] recently reported that of 136 infants with tetany, 68 per cent were males. The other two diseases, pyelitis and primary peritonitis, occurred predominantly in females, no less than 80 per cent of the patients with pyelitis and 75 per cent of the patients with primary peritonitis being females. It has been suggested by some surgeons that primary peritonitis occurs exclusively in females and that errors in diagnosis account for the diagnosis in male patients.

Endocarditis and chorea occurred more frequently in females, 57 per cent females with endocarditis and 61 per cent females with chorea. Curiously enough only 40 per cent of the cases of rheumatic fever occurred in females.

Whooping cough and typhoid are the only other diseases that occurred more frequently in females than in males.

TABLE 4.—*Sex Incidence of Disease*

Disease	Total Number	Males, per Cent	Females, per Cent
Pyloric stenosis	100	82	18
Tetany	89	68	32
Pyelitis*	228	20	80
Primary peritonitis	32	25	75
Endocarditis	351	43	57
Chorea	188	39	61
Rheumatic fever	108	60	40
Whooping cough	162	41	59
Typhoid*	82	46	54

* The records from a former series reported from this hospital are included.

In a recent review of the literature on Meckel's diverticulum as a cause for intestinal hemorrhage,[9] twenty-six cases were found. It is of interest to note that in twenty-five of these cases the patients were males.

Seasonal Incidence.—Tetany and anterior poliomyelitis are the two diseases with most marked seasonal incidence. Eighty per cent of the patients with tetany were encountered during the months of February, March, April and May, and no less than one third of the total occurred during March alone. No cases were observed during July, August and September. Seventy-two per cent of the patients with anterior poliomyelitis were encountered during August, September and October, and only 3 per cent during January, March, April and May.

8. Bakwin, H., and Bakwin, R. M.: Sex Factor in Infantile Tetany, Am. J. Dis. Child. **35**:964 (June) 1928.

9. Tisdall, F. F.: Unusual Meckel's Diverticulum as Cause of Intestinal Hemorrhage, Am. J. Dis. Child. **36**:1218 (Dec.) 1928.

Retropharyngeal abscess, nephritis, erysipelas and primary peritonitis have been grouped together, because they all occur predominantly during the first six months of the year. This would suggest some common factor in their production, such as the prevalence of infections of the upper respiratory tract at this time of year coupled with a probably lowered resistance due to a lack of sunshine.[10] For many years we have recognized the close association of infections of the upper

TABLE 5.—*Seasonal Incidence of Disease*

Disease	January	February	March	April	May	June	July	August	September	October	November	December
Tetany	3	13	30	19	10	7	0	0	0	1	1	5
Anterior poliomyelitis	0	1	0	1	1	5	10	25	29	25	9	3
Typhoid	0	0	0	1	2	2	2	1	5	2	0	3
Retropharyngeal abscess	12	11	12	6	6	7	4	3	1	0	6	4
Nephritis	9	16	16	8	12	8	8	4	2	8	8	10
Erysipelas	28	13	33	18	25	10	12	14	9	6	11	16
Primary peritonitis	7	1	3	2	7	5	2	0	0	3	1	1
Acute appendicitis	25	26	35	30	23	24	24	27	43	34	30	29
Intussusception	2	5	8	6	12	7	11	11	8	13	5	8
Pyloric stenosis	3	6	10	2	8	10	10	12	17	8	5	9
Pyelitis	10	5	9	10	8	12	11	16	19	7	16	8
Hemorrhagic disease of newborn infants	7	14	9	13	7	6	8	3	3	4	8	5
Purpura	2	3	4	4	2	1	1	2	2	2	2	3
Living births in Toronto from 1923 to 1927 (figures are in hundreds)	51	48	50	54	55	54	57	56	51	51	45	47
Chickenpox	1478	763	703	464	492	879	575	229	235	782	2152	1709
Scarlet fever	964	878	893	700	736	523	288	178	213	409	618	755
Measles	1781	1649	2165	2211	2766	2024	1336	341	153	561	1086	1433
Whooping cough	441	441	458	402	480	447	509	402	463	350	356	286
Endocarditis	36	33	37	28	34	35	23	13	25	29	27	31
Rheumatic fever	8	7	10	12	5	10	20	5	3	9	8	11
Chorea	20	14	15	19	18	19	20	16	15	10	7	15
Eczema	6	7	12	6	7	9	7	6	5	3	8	7
Asthma	2	3	1	2	4	1	4	4	7	7	4	1
Diabetes	6	11	9	9	7	9	4	7	9	6	6	0
Epilepsy	10	1	12	11	12	11	14	5	12	14	14	9
Acrodynia	2	4	2	0	1	2	1	3	4	1	1	0
Scurvy	3	4	1	7	1	3	1	4	6	4	8	6

respiratory tract and acute nephritis and also the rapidity with which the nephritis in many patients clears up following the removal of infected tonsils. With this in mind it is of interest to note the frequent occurrence of this condition during the winter and spring months. Primary peritonitis occurred only twice in July and not at all in August and September; this would indicate no connection with the gastro-intestinal disturbances prevalent during the summer months. Appendicitis on the other hand, although prevalent during the winter and spring, occurred most frequently during September.

10. Robertson, E. C.: Canad. M. A. J. **19**:154, 1928.

Intussusception, pyloric stenosis and pyelitis all occurred more frequently during the summer and early fall than during the winter. At first one might expect pyelitis to be more closely associated with the infections of the upper respiratory tract which are frequent during the winter months. The infecting organism, however, is almost invariably the colon bacillus, which is what one would expect if there was some connection with gastro-intestinal disturbances. Our figures lend weight to this possibility. What connection there can be between gastro-intestinal disturbances and congenital hypertrophic pyloric stenosis or just why this condition should occur more frequently in the summer than in the winter is not evident.

Hemorrhagic disease of the new-born and purpura occured most frequently during the winter months. McCollum [11] directed attention to this seasonal incidence of hemorrhagic disease of the new-born and suggested some association of a lack of ultraviolet rays during this period of the year with the tendency to hemorrhage. Sooy and Moise [12] made the assertion that exposure of patients to ultraviolet rays increases the blood platelets.

In regard to chickenpox, scarlet fever, measles and whooping cough, chickenpox occurred most frequently during November, scarlet fever during January, measles during May and whooping cough during July. A point of considerable practical importance is that while most respiratory conditions and infections of the upper respiratory tract productive of coughs are seen least frequently during the summer months, whooping cough, on the other hand, is encountered with slightly greater frequency during the summer than during the winter. A persistent cough during the summer months is thus suggestive of whooping cough.

In view of the association of tonsillar infections with endocarditis, rheumatic fever and chorea, it is surprising that these diseases do not occur predominantly during the winter months.

Asthma occurred most frequently during the summer and fall, in contradistinction to eczema, with which it is closely associated and which occurs with almost equal frequency throughout the year.

SUMMARY

1. The records of nearly 2,500 patients admitted to the Hospital for Sick Children and about 5,000 records obtained from the Toronto Department of Public Health have been examined to determine the age, sex and seasonal incidence in various diseases.

11. McCollum, J. L.: Canad. M. A. J. **18**:550, 1928.

12. Sooy, J. W., and Moise, T. S.: J. Lab. & Clin. Med. **12**:113, 1927.

2. The diseases considered are endocarditis, rheumatic fever, chorea, scurvy, tetany, intussusception, hemorrhagic disease of the new-born congenital hypertrophic pyloric stenosis, purpura, erysipelas, pyelitis, acrodynia, primary peritonitis, appendicitis, typhoid, retropharyngeal abscess, nephritis, diabetes mellitus, eczema, asthma, anterior poliomyelitis, chickenpox, scarlet fever, measles and whooping cough.

3. A pronounced age incidence was observed in the following diseases; endocarditis, rheumatic fever, chorea, scurvy, tetany, intussusception, hemorrhagic disease of the new-born and acrodynia.

4. In the majority of the diseases considered, we found that the males constituted no less than 60 per cent of the total patients affected. This figure is singularly constant, although of the living infants born in Toronto from 1923 to 1927, the males constituted slightly more than 50 per cent of the total.

5. There are four diseases which occurred predominantly in one or the other sex. Pyloric stenosis and tetany occurred chiefly in males, while pyelitis and primary peritonitis occurred predominantly in females. Endocarditis, chorea, whooping cough and typhoid were the only other diseases seen more frequently in females than in males.

6. A marked seasonal incidence was noted in only two diseases: tetany and anterior poliomyelitis. Retropharyngeal abscess, nephritis, erysipelas, primary peritonitis and acute appendicitis occurred somewhat more frequently during the winter and spring months; this is suggestive of an association with infections of the upper respiratory tract.

Pyelitis, intussusception and pyloric stenosis, on the other hand, were noted more frequently during the summer; this suggests some connection with the gastro-intestinal disturbances so prevalent at that period of the year. Whooping cough occurred as frequently in the summer as in the winter. A slight but definite seasonal predominance was found with hemorrhagic disease of the new-born, purpura, chickenpox, scarlet fever, measles and asthma.

RESUSCITATION OF ASPHYXIATED NEW-BORN INFANTS *

ROLAND S. CRON, M.D.

MILWAUKEE

Methods of resuscitation of asphyxiated new-born infants as practiced at the present time are more nearly like those of the dark ages than any other procedure in medicine. Mathieu and Holman [1] compared them to a chapter from "Mother India," while Henderson [2] stated that "no single discovery in medical science or improvement in practice could do more to save lives than would measures to avoid the losses that now occur within a few minutes after birth." The reason for this situation can be found in the statements contained in textbooks of physiology and obstetrics. In such accounts, stress is laid on the effects of counter-irritation, or shock, as accomplished by vigorous slapping, plunging the infant into ice-cold water, swinging the infant by the feet through the air, dilating the rectal sphincter, and in general, squeezing, hauling and manhandling. Breathing is supposed to be initiated by these procedures, but in fact the child may be so injured that it will never breathe, or if it does, it may later die from a ruptured viscus or blood vessel. Mathieu and Holman are undoubtedly correct when they state that these infants live in spite of such treatment.

For years, teachers of physiology have tried to impress on physicians the fact that respiration is controlled by the chemical state of the blood, and its effect on the respiratory center. Before birth, the fetus does not attempt to breathe because the exchange of respiratory gases in the blood is such as does not stimulate respiration. Henderson stated:

> After birth the infant breathes in response to the same stimulus and by the same mechanism as those which the modern physiology of respiration has shown obtained in adults, in children, and in all mammalian animals. In all these, and in the infant no less, the maintenance and regulation of breathing depend on the carbon dioxide brought to the respiratory center in the blood. Oxygen is requisite if the center itself is to be maintained in normal condition, and if the tissues are to produce carbon dioxide, for deprivation of oxygen necessarily decreases the production of

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* From the Department of Obstetrics and Gynecology, Marquette University.

1. Mathieu, Albert, and Holman, Albert: Resuscitation of the Asphyxiated New-Born, J. A. M. A. **92**:1917 (June 8) 1929.

2. Henderson, Yandell: The Prevention and Treatment of Asphyxia in the New-Born, J. A. M. A. **90**:583 (Feb. 25) 1928.

carbon dioxide. But the center may be quite normal and also quite inactive in the presence of ample oxygen if the blood is deficient in carbon dioxide. If the center has become inactive, or if its activity is subnormal, there is one, and only one, stimulus that will both restore and maintain normal activity: an increase of carbon dioxide in the blood. . . . It is as certain as anything in the whole range of modern science that respiration is under a chemical control by the more or less direct action of the arterial blood, chiefly through its content of carbon-dioxide, on the respiratory center in the brain. It has been proved also that oxygen is not a stimulant, a fact which clinicians seem to find extremely hard to appreciate. . . . Asphyxia is usually thought of as a condition of oxygen deficiency and excess of carbon dioxide. This is a misconception; asphyxia usually, as in the typical condition of carbon monoxide poisoning, involves both low oxygen and low carbon dioxide content in the blood and tissues. . . . It is the carbon dioxide carried by the blood from the tissues to the brain that is the physiologic stimulant to respiration. When the center is depressed, it requires more than the normal amount of this stimulant to induce activity.

Before any attempt is made to correct this carbon dioxide and oxygen deficiency, the amniotic fluid and other detritus must be cleared from the mouth, larynx, trachea and bronchi. As is witnessed at the time of delivery, usually the birth over the perineum and accompanying compression of the chest squeezes most of this fluid out. In the case of breech deliveries and cesarean sections, such compression does not occur and removal by artificial means is required. Infants dying of pneumonia directly after birth show, on section, bronchioles and alveoli filled with amniotic fluid and epithelial cells. If these are sterile, they are absorbed without much disturbance; but if the infants have breathed or have received mouth to mouth insufflation, they are usually infected and at autopsy a pneumonia will be found with evidence that the contents of the air passages have been forced into the small air radicles. Flagg [3] stated that a positive pressure of from 50 to 70 mm. of mercury is all that is necessary to bring this about.

A number of methods of artificial resuscitation for the asphyxiated new-born infant have been advocated during the past year by physiologists and obstetricians. Certain facts in the treatment of these infants have been agreed on: 1. There should be no increase in the cerebral ischemia and resultant depression of the respiratory center. This can be accomplished by handling the infant in a most gentle manner, and placing it in a medium with a temperature similar to that from which it was just expelled. No spanking, compression of the chest against the symphysis, dilatation of the rectal sphincter or immersion in cold tubs of water should be used. 2. The air passages, mouth, pharynx and larynx must be cleared of mucus, amniotic fluid, epithelial cells and blood before resuscitation is attempted. 3. Oxygen and carbon dioxide

3. Flagg, P. J.: Treatment of Asphyxia in the New-Born, J. A. M. A. **91**:788 (Sept. 15) 1928.

(5 per cent) should be introduced, or at least made available for use by the smaller air radicles of the asphyxiated new-born infant.

Various instruments have been designed by both the physiologist and the obstetrician. Frequently the physiologist has overlooked the practical side of the subject and has attempted to introduce an armamentarium too complicated for the clinician. It must be kept in mind that the physician, whether he be a general practitioner or an obstetrician, is qualified to use only the simplest technic. Such apparatus as suggested by Flagg is impractical in the hands of any one excepting the trained laryngologist. Furthermore, it is too expensive for even the average hospital, and especially for the general practitioner to own.

The technic, with modifications, which has been found most effective has been similar to that advocated by Henderson. As soon as the infant's head is born, any débris is removed from the mouth and both nares by means of the common rubber ear bulb so that the first inspiration will not draw foreign material into the lungs. After the infant is born, and before the cord is cut, the infant is suspended by the feet, and the trachea and larynx gently milked toward the mouth. Again, the compressed bulb is introduced into the mouth and nares and all foreign material removed. The infant is than placed on its right side, and amniotic fluid, blood and vernix caseosa are gently wiped off. This is the best and only type of external stimulation used. Usually this is sufficient to initiate a cry and normal respirations. As soon as pulsations have ceased, the cord is cut. The infant and ear bulb are placed in a warm blanket and handed to the nurse, who places them in the crib. If after a short time, and following cleansing and drainage of the air passages, the infant does not make attempts at respiration it is placed in a tub of warm water, and the McKesson infant inhalator applied to the infant's nose and mouth. The inhalator is supplied with a tank of oxygen containing 5 per cent carbon dioxide. The escaping gas is controlled by means of a needle valve and should be regulated so that its outflow can just be felt when the mask is applied to the operator's face. The physician then gently compresses the infant's chest with the palm of the hand so as to force out the air from the infant's lungs. Due to the natural resiliency of the thoracic wall, the mixture of oxygen and carbon dioxide is then drawn into the lungs as the compression is released. Synchronous with the release of the infant's thorax, the escape valve to the mask is obstructed by the nurse's thumb and positive pressure assists in carrying the mixture into the air spaces. The same technic is carried out with each successive inspiration until respiration is well established.

This method of resuscitation has been successfully used in many hundreds of asphyxiated new-born infants. However, great care must

be observed in having the air passages unobstructed and that the oxygen and carbon dioxide escape at a pressure too low rather than too high. The method described has rarely proved ineffective. Evidence of its ineffectiveness is marked retraction at the costal margins during inspiration without lessening of cyanosis. Likewise, when mucus, amniotic fluid and débris are especially abundant, or in the absence of the apparatus mentioned, one should resort to the use of the tracheal catheter. I have adopted the technic as described by Mathieu and Holman, and have taken the liberty to quote from their essay:

> The baby, wrapped in a warm blanket, is placed with its head over the edge of a table. The head is steadied by an assistant. After sterile water has been drawn into the catheter to prove its patency, the index finger of the right hand depresses the tongue and at its base locates the tiny slit that is the opening into the larynx. The small fiber catheter is inserted with the left hand, so that its tip eventually finds itself beneath the end of the finger at the small slit opening into the larynx. Then, by slight depression of the tip of the catheter with the index finger of the right hand, the catheter readily finds its way into the opening of the larynx. The position of the catheter can be easily proven by advancing the finger of the right hand slightly into the esophagus. The catheter is inserted 3 or 4 cm. farther and suction is made to extract mucus from the larynx and upper trachea. The catheter is then removed and cleared by blowing through it. The catheter is again inserted into the trachea and artificial respiration is started.
>
> The lungs are in a state of atelectasis, a condition in which there has been no inflation of the pulmonary tissues; the alveoli are collapsed, and the bronchi and small bronchioles have their walls in a state of physiologic adhesion. The first impulse through the catheter should be gentle and of small volume. As the tidal air in the respiration of the average new-born child is only 45 cc., the first inflation through the catheter should be not more than from 10 to 15 cc. and the subsequent ones gradually increased. This calls for nicety of judgment on the part of the operator and is the only part of the maneuver in which there is likelihood of doing gross harm to the infant. In the new-born infant, the respiration is at first diaphragmatic because of the weakness of the intercostal muscles and the horizontal position of the ribs. Breathing is shallow, because in a recumbent position the abdominal viscera press firmly against the diaphragm; hence, it is approximately from 40 to 45 inspirations a minute. There is no pause between inspiration and expiration or between expiration and inspiration. Bearing these facts in mind, the operator should puff, very gently, into the catheter through the trap about forty times a minute in order to simulate as closely as possible the normal respiration of the new-born. The force to be used would, with the lips pursed to whistle, be felt on the wet finger about 3½ to 4 inches (9 or 10 cm.) from the mouth, or would be about the same force one would use in blowing small smoke rings.

The more pronounced the asphyxia, the easier is the intratracheal insufflation owing to the fact that with absent reflexes the glottis is from two to three times larger. The opposite is also true, the easier the introduction of the catheter the greater is the indication for that method of resuscitation.

SUMMARY

1. A new-born infant who fails to breathe, or is asphyxiated, should not be treated by the old-fashioned method of cutaneous shock or stimulation. Such methods are harmful and may add to the already present cerebral ischemia.

2. Oxygen is a food, not a stimulant. Carbon dioxide is a stimulant to the respiratory center. In the absence of oxygen the tissues of the body cannot produce carbon dioxide. When the center is depressed, additional carbon dioxide must be administered to induce its activity.

3. No attempt at artificial respiration should be made until the air passages have been cleared of amniotic fluid, mucus, blood and other detritus.

4. The administration of oxygen and carbon dioxide can be accomplished by means of the pressure inhalator with manual compression of the infant's thorax, or by means of the intratracheal catheter utilizing the physician's expired breath. This air contains about 5 per cent carbon dioxide and 20 per cent oxygen, sufficient for stimulation and proper foodstuff.

Pediatric Biographies

JOHN PECHEY
1655-1718

JOHN RUHRÄH, M.D.
BALTIMORE

Every student of Sydenham is familiar with what, if it is not the best, is at any rate the most readable English translation, that by John Pechey, and it is on this that the latter's fame chiefly rests. Few indeed are there who know that Pechey wrote a good book on the diseases of children, not to mention other publications of more or less interest.

There were two Johns of nearly the same name. This has led to some confusion which has been cleared up by G. C. Peachey.[1] The name was originally Peche, and various members of the family spelled it differently. The two Johns were descended from different branches of the family. John Peachi received his M.D. in Caen, practiced in Gloucestershire and was extra urbem licentiate of the College of Physicians. The other John was the son of William Pechey, of Chichester, himself a practitioner of medicine and surgery. John was sent at the age of 17 to New Inn Hall at Oxford from which he was graduated, receiving his B.A. in 1675 and his M.A. in 1678. There is no evidence that he ever received a doctor's degree in medicine although some of the later editions of his Sydenham have added M.D. to his name. He probably returned to Chichester to study with his father, and later he went to London. He applied for a license of the College of Physicians in 1684, and after three examinations toward the end of the year he was admitted to license. In 1687, he took a lease in connection with two other physicians on part of a house in Cheapside known as The Golden Angel and Crown. These three apparently started a dispensary, probably the first in London. This "Repository" was in direct opposition with the scheme of the relief of the sick poor of the College, and it doubtless had something to do with their treatment by the College later.

In November, 1688, it is recorded in the Annals of the College that Pechey was summoned to appear before the Censors "Upon printing bills signifieing his removal and shilling fee and putting up a board of notice to the people with his name over his dore, (upon which) he was admonished and put off till next meeting." A month later he was fined

1. Peachey, G. C.: The Two John Pecheys, Janus **23**:121, 1918.

A General

TREATISE OF THE DISEASES OF Infants and Children.

74209.

Collected from the best

PRACTICAL AUTHORS.

By *JOHN PECHEY* of the College of Physicians in *London*.

LONDON:

Printed for *R. Wellington*, at the *Lute* in *St. Pauls-Church-Yard*. 1697.

4 pounds because he continued *spargere cartulas* (to distribute his bills) and had not removed the board from his dore. He was subsequently fined 8 pounds, and he also did not pay his 40 shillings dues to the College. It was ordered that he be sued for them, but apparently nothing was done, and he, along with others, took the oath of allegiance and signed the declaration required by Parliament, his signature appearing as "Joh. Peachey."

It is probable that he moved to Basing Lane, and the house was called "The Angel and Crown"; it is also probable that the partnership was dissolved. The article in *Janus* contains the following:

In November, 1693, he issued the following advertisement in "The Athenian Mercury": "At the Angel and Crown in Basing Lane, being the 2nd turning in Broad St. from Cheapside on the left hand, the sick may have advice for nothing and excellent purging pills prepared by J. Peachy of the College of Physicians in London,—here follows a long description of their virtues—in tin boxes containing 18 pills, price 1/6; my Elixir for the Stone and Chollick price 2/6, and approved medicines for the cure of other diseases," etc.

And as if to excuse himself for what he knew was unprofessional and dishonouring, he added:— "Many ill men make it their business to reproach the Public way of practice because it thwarts their private interests." In his "Treatise of Aploplexy printed privately for the author in 1698, and sold at his house in Basing Lane, he surpassed himself with a full description of his secret remedies, ten in all, down to his Worm Powders at 4^{d} each: and we get a further insight into his methods of practice from an advertisement which he inserted in several newspapers during the month of January, 1700:

"At the Angel and Crown in Basing Lane, near Bow Lane, lives J. Pechey, a Graduate in the University of Oxford, and of many years standing in the College of Physicians in London; where all sick People that come to him may have for six Pence a faithful Account of their Diseases and plain Directions for Diet, and other things they can prepare themselves. And such as have occasion for Medicines may have them of him at very reasonable Rates without paying anything for Advice. And he will visit any sick Person in London or the Liberties thereof in the day-time for two Shillings and six Pence, and anywhere else within the Bills of Mortality for five Shillings. And if he be called in by an Person as he passes by in any of these places, he will require but one Shilling for his advice."

He was reprimanded by the College and by his fellow practitioners, but in spite of the threats of the College and his order to be prosecuted apparently nothing came of it.

His name does not appear in the 1716 catalogue of the College. He died in 1718.

His best known work is his translation of Sydenham, which first appeared in 1696 and went through eleven editions, the last of which is dated 1740. In addition, he published "Collections of Acute Diseases in Five Parts," 1686 to 1691, and "A Collection of Chronical Diseases, 1692." Then followed "The London Dispensatory" and "The Com-

pleat Herbal" 1694, and "The Storehouse of Physical Practice," 1695. "A General Treatise of the Diseases of Maids, Big Bellied Women, Childbed Women and Widows" appeared in 1696 and "A General Treatise of Diseases of Children" in 1697. These were followed by several other publications.

The work on the diseases of children is a 12mo of 160 pages and contains the following chapters:

Chap.
I. Of the Dyet and ordering of Children New-born
II. Of the Diseases and Symptoms of Infants in General
III. Of the Fevers of Children
IV. Of the Small-Pox
V. Of the Measles
VI. Of Scabs and Ulcers from Milk
VII. Of a Tinea
VIII. Of the Lowsie Disease
IX. Of an Hydrocephalus and Inflation of the Head
X. Of a Siriasis
XI. Of Frights in Sleep
XII. Of Watching
XIII. Of Children's Convulsions
XIV. Of Squinting
XV. Of the Pain, Inflammation, Moisture, Ulcers and Worms of the Ears
XVI. Of Aphthae, Bladders, of the Gums and an Inflammation of the Almonds
XVII. Of Breeding Teeth
XVIII. Of Loosening the String of the Tongue, and of the Ranula of the Tongue
XIX. Of a Catarrh, Cough and Difficulty of Breathing
XX. Of the Hichop
XXI. Of Vomiting
XXII. Of the Gripes
XXIII. Of the Inflation of the Belly and Hypochondres
XXIV. Of a Looseness
XXV. Of Costiveness in Children
XXVI. Of Worms
XXVII. Of Rupture
XXVIII. Of the Sticking out of the Navel
XXIX. Of an Inflammation of the Navel
XXX. Of the Falling of the Fundament
XXXI. Of the Stone in the Bladder
XXXII. Of the Difficulty and Retention of the Urine
XXXIII. Of Incontinence of Urine
XXXIV. Of the Galling of Children
XXXV. Of the Rickets
XXXVI. Of Children Wasting

This text is full of sound sense and is a good outline of the practice of the time. In the preface he wisely remarks:

To conclude the young Physician must take Notice that great caution must be used in prescribing Opiates and Vomits for Children, for many dreadful Symptoms have been occasioned thereby.

The first chapter is "Of Dyet and ordering of Children New-born," and in this he wrote:

As Galen says in another place, much less is the custom of some barbarous people to be imitated, which was also used formerly in Germany. The dipping the warm infant from the womb in the next Brook, that thereby it may be rendered more strong and lusty, and to try the strength of their children, whom they chiefly design for the Wars; for without doubt none but strong children would survive such a dipping.

Other extracts are as follows:

Most commonly children do not cry without a cause, but are provoked by something which disturbs them, a Provident Mother or Nurse will endeavor to find out what is the cause, that that being removed the child may be a quiet: She will see whether the Linnen be foul'd for Children love to be clean and will not sleep quietly till filthy close are removed from them: the Mother will see whether they are swathed too hard, or whether they are not pinched by a pin, or whether gripes be the occasion. . . . After some months you may feed the Child with Pap. . . . But it is not convenient to give solid meats before they have Teeth for they cannot chew them:

OF THE FEVERS OF CHILDREN

The first indications in curing Children's Fevers is to prepare well the acid, that it may be the easier ejected, but this preparation must not be Endeavoured by Sudorificks, properly so called, that is such that heat the body, which are no means to be used for Infants or Children; but such things as absorbs the acid, and gently restrain the Ebullitian, are to be used, the chief of these are crabs Eyes and Claws, Oyster shells, Cuttle-bones, Egg shells, Coral, Coaline, Pearl, Mother of Pearl, both the Bezoarstones, Harts-horn burnt, burnt Ivory, the Bone of a Stag's heart, Shavings of Harts-horn, Bolearmonick, Seald-Earth, Blood stone, and the like and among compounds, compound powder of Crab's Claws, the Goastone, and the confection of Hyacinth.

He gives a good account of smallpox and also "meassels":

Children are chiefly subject to these ill symptoms, which appear now at the going off of the Measles, by reason of two hot a Reginen, or hot Medicines, that were used to force them out, and by this means they are cast into a Peripneumonia, which destroys more than the small-pox; and yet the measles are not at all dangerous, if they are skillfully managed.

He makes a most interesting statement concerning the use of alkalis, and remember this was in 1697:

But it is here to be noted, the Gripes, Restlessness, and Watchings of Children are as easily appeased by testacious Powders as Pains and Watchings by Narcoticks in grown people.

He also knew and recommended rhubarb a good drug, somewhat neglected in pediatric practice at the present time:

There is no purging Medicine more proper for Children, and more innocent than Rhubarb, it gently and safely evacuates the matter occasioned by the Fever, and gently purges off the Humours, that burthen the Stomach and the Whole Body, and it strengthens. Wherefore it is very proper for Infants, Children, big bellied women, Old Men, and such as have been weakened by Diseases.

The prevalence of vermin at the time may be gathered from the following:

OF THE LOWSIE DISEASE

The grown people, if they live nastily and wear foul Cloaths, and do not change often their Woolen, as well as their Linnen, are subject to lice, yet this nasty disease is most familiar to Children, nor can Gentlemen's Children be free from them, for they breed in their Heads.

Numerous remedies follow.

In common with others writing on the diseases of the young he includes a chapter on ranula. It may be questioned whether these fungoid growths as here described were not something like Riga's or Fede's disease, where the growth is doubtless due to some infection.

As to the Ranula under the Tongue, there are large and conspicuous Veins under the Tongue, which are sometimes filled with ill blood; therefore if a flegmatick humour be gathered here, and sweats out thence, and sticks there without passage of the flesh, a tumour is occasioned by it and the blood like a Fungous generated upon a Tree; and if it continue long and increase, it hinders the speech; and therefore ought to be timely remedied; wherefore the tumour is to be removed by the application of Salt and Frankencese mixed, or with powder of Sage mixed with honey of Roses and a drop or two of spirit of Vitriol or Take of Cuttle bone, Sal Gemma and Pepper, each one dram; of burnt spunge three drams; make a powder, wherewith rub the tumour or with the foregoing powder and honey make a Linement, and anoint the tumor with it, and apply under the chin a Plaister made with equal parts of Goose-dung and honey boyled in Wine to the consumption of the Wine.

News and Comment

GENERAL

International Pediatric Congress. — The American pediatric profession should know that the subjects to be chosen for special consideration at the International Pediatric Congress, to be held in Stockholm, Aug. 17 to Aug. 20, 1930, have not as yet been announced. These will constitute only a portion of the program. All papers must be approved by the Committee before March 1. The following is quoted from a communication from Dr. I. Jundell:

"As to the lectures, we have no intention of limiting their number, as we feel that this might give rise to bad feeling in one quarter or another. The only limitation we have hitherto planned is that of novelty. We request that no lectures previously given or published be repeated at the conference.

"Should the number of lectures proposed nevertheless be too large, the necessity may arise of requesting the national committees of the respective countries to make a choice from among the lectures of their own countrymen."

Those who wish to read papers at the International Congress should apply to one of the members of the American Committee, which is composed of:

Dr. Kenneth D. Blackfan, 300 Longwood Ave., Boston.
Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Dr. Alfred F. Hess, 16 W. 86th St., New York.
Dr. Julius H. Hess, 104 S. Michigan Blvd., Chicago.
Dr. William P. Lucas, 490 Post St., San Francisco.
Dr. Hugh McCulloch, 500 S. Kingshighway Blvd., St. Louis.
Dr. Edwards A. Park, Johns Hopkins Hospital, Baltimore.
Dr. Clifford G. Grulee, Chairman, 310 S. Michigan Blvd., Chicago.
Dr. Charles A. Aldrich, Secretary, 545 Lincoln Ave., Winnetka, Ill.

Each one so applying should state his name, address and the title and content of his thesis. Professor Jundell has requested that all papers coming from each country be approved by the committee of that country.

The Heckscher Institute for Child Health.—The Heckscher Foundation created the Heckscher Institute for Child Health on Fifth Avenue and One Hundred and Fourth Street, New York, as a central organization, both academic and practical, for the early recognition and prevention of disease and defectiveness in childhood. Dr. I. Newton Kugelmass, New York, will direct the work of the Institute with a group of leading physicians representative of the hospitals of the city and with the guidance of a distinguished advisory board. The members of the Advisory Board are Dr. Frederic H. Bartlett, Dr. William H. Park, Dr. Frederick B. Robinson, Mr. Robert Rust, Dr. Bela Schick, Dr. Homer W. Swift, Dr. Herbert M. Wilcox, Dr. Wiley E. Woodbury, Dr. Helen T. Wooley, Dr. Shirley W. Wynne and Mr. August Heckscher, ex officio.

The heads of the Departments devoted to child health are: Dr. Robert Cooke, the New York Hospital, in charge of the allergy clinic; Dr. Frederic W. Bancroft, the Fifth Avenue Hospital, in charge of the surgical clinic; Dr. Ernest P. Boas, Mount Sinai Hospital, in charge of the cardiac clinic; Dr. George MacKee, the Post-Graduate Hospital, in charge of the skin clinic; Dr. Carl P. Sherwin, the Fordham Hospital, in charge of the immunization clinic; Dr. Josephine B. Neal, the Willard Parker Hospital, in charge of the infectious diseases department; Dr. A. I. Ringer, the Montefiore Hospital, in charge of the metabolic clinic; Dr. Westley M. Hunt, the Fifth Avenue Hospital, in charge of the nose and throat clinic; Dr. James W. Smith, the Knapp Eye Hospital, in charge of the eye clinic; Dr. Royal S. Haynes, the Presbyterian Hospital, in charge of the posture clinic; Dr. John S. Greene, the Hospital of Speech Disorders, in charge of the speech clinic; Dr. Jesse G. Bullowa, the Harlem Hospital, in charge of the chest clinic; Dr. Robert E. Pound, the First Avenue Hospital, in charge of roentgenology; Dr. Mary S. Rose, Teachers College, in charge of nutrition; Dr. William L. Sneed, the Ruptured and Crippled Hospital, in charge of orthopedics;

Dr. Harold Nagel, the Polyclinic Hospital, in charge of stomatology; Dr. Thomas T. Mackie, the Presbyterian Hospital, in charge of the child structure clinic; Dr. Ralph H. Brodsky, Mount Sinai Hospital, in charge of the dental clinic; Dr. Margaret Fries, the Women's Infirmary, in charge of the behavior clinic, and Dr. B. S. Barringer, the Fifth Avenue Hospital, in charge of urology.

Bequests to Children's Hospitals.—The County Home for Convalescent Children and the Home for Destitute Crippled Children have been given $92,000 each, by the will of the late William Liston Brown, formerly of Chicago, who died in California.

The First International Congress on Mental Hygiene.—This congress will be held at Washington, May 5 to 10, 1930. Some of the subjects to be discussed are those of problems of special type children, methods and possibilities of child guidance, and the significance of parent-child and teacher-child relationships.

Diphtheria Immunization in Brooklyn.—In the campaign against diphtheria in New York, Brooklyn leads all the other boroughs; 201,698 children have been immunized during the year.

West Virginia Child Health Conference.—The conference was held at Morgantown on November 26. Among the speakers was Harry E. Barnard of Washington, D. C., director of President Hoover's conference on child health.

UNIVERSITY NEWS

Columbia University has received $90,000 from the Laura Spelman Rockefeller Memorial for the Child Development Institute as a gift to Teachers College.

The faculty at the Harvard University School of Medicine, Boston, announce the appointments of Dr. Frank R. Hopkins and Dr. Arthur R. Turner as assistants in pediatrics, and Dr. Frederick M. Spencer as research fellow in pediatrics.

Dr. Florence Mabel Holsclaw of San Francisco died on October 30, at the age of 57. She graduated from Cooper Medical College, San Francisco, in 1907. She was associate clinical professor of pediatrics, University of California Medical School, formerly assistant clinical professor of medicine and pediatrics, Stanford University, School of Medicine, and for many years was on the staff of the Children's Hospital. She contributed many articles to pediatric literature, some of which were published in the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

SOCIETY NEWS

Philadelphia Pediatric Society.—The Philadelphia Pediatric Society, which has approximately 400 members, has instituted a biennial prize competition. The object of the competition is to stimulate active interest in pediatrics among recent graduates. It is limited to physicians practicing in the metropolitan area of Philadelphia, who have not been graduated more than six years. Investigations are permitted the broadest scope, except that they must pertain to pediatric subjects. The first prize is $100, and a second prize of $50 has been offered if in the opinion of the judges the investigations submitted are of sufficient merit. The papers for the first biennial prize competition must be in the hands of the secretary on or before Oct. 1, 1930.

Chicago Medical Society.—The Chicago Medical Society has recommended to Dr. Arnold H. Kegel, health commissioner of Chicago, that practicing physicians will make diphtheria toxin-antitoxin injections on Saturdays at $1.00 each. It is planned to reach every precinct to advise parents to have their children immunized.

Nebraska Pediatric Society.—The name of the Nebraska-Iowa Pediatric Society has been changed to the Nebraska Pediatric Society, in accordance with the recommendation of the pediatric section of the American Medical Association. Efforts are being made to carry out other recommendations of the section.

Obituary

HARRY MONROE McCLANAHAN, M.D.
1856-1929

Dr. Harry Monroe McClanahan died on Nov. 20, 1929, at Omaha.

Dr. McClanahan, son of Dr. John Porter and Margaret Jane (Jones) McClanahan, was born at Norwood, Mercer County, Ill., on Aug. 17, 1856. He received his early education in and was graduated from Monmouth College, Monmouth, Ill., receiving his A.B. degree in 1875; he attended the Jefferson Medical College, Philadelphia, and received the degree of M.D. in 1878. On Sept. 6, 1883, he married Nellie E. Holloway of Alexis, Ill.

Dr. McClanahan held the following positions: He was resident physician of Jefferson Medical College from 1878 to 1879; he practiced at Alexis from 1879 to 1880, was agency physician at Fort Belknap, Mont., from 1880 to 1881 and practiced at Woodhull, Ill., from 1881 to 1889. In 1889, he came to Omaha, where, in 1892, he became Professor of Pediatrics at Omaha Medical College (now University of Nebraska College of Medicine). In 1927, he was made Professor Emeritus, but continued to hold clinics and to lecture to the senior class up to the time of his death. He was a member of the American Medical Association, (holding the office of vice president in 1912, and acting as chairman of the Section on Diseases of Children from 1901 to 1902), American Pediatric Society, American Society for the Study and Prevention of Infant Mortality, American Teachers of Diseases of Children (president from 1914 to 1915), Nebraska State Medical Society (president, 1912), Fellow American College of Physicians, Phi Rho Sigma and Alpha Omega Alpha.

Dr. McClanahan's life was an active one from the time he graduated in medicine, and he was always endeavoring to impart to others the knowledge obtained from his observations and work. He was a regular attendant at the meetings of the various national societies and endeavored throughout his life to keep up with the present trend of medicine. When others took vacations, Dr. McClanahan spent his time at the various clinics, medical societies and abroad to further his education along the lines of advanced medicine.

The first article published by him was in the *Medical and Surgical Reporter,* volume 44, March 26, 1881, on "The Practice of Medicine Among the Indians." He contributed several articles during the year

1881 along this line. About fifty articles dealing with pediatric problems were written and published in various journals during his life. In his seventieth year, he wrote and completed his book on "Pediatrics for the General Practitioner," which was published Jan. 1, 1929, by the J. B. Lippincott Company. In all of the papers written and also in the book published by Dr. McClanahan, the general practitioner was always kept in mind.

My own intimate association with him, both in a professional way and in the home, dates back fifteen years and enables me to testify to those qualities which endeared him to all members of the medical profession and to the parents and children whom he had the privilege of having under his care.

He was one of the best and fairest of consultants, and was conscientious in the use of opiates in his practice. He neither smoked nor drank, and was a devout Christian gentleman, a regular attendant at the Presbyterian church. To Dr. McClanahan the home was sacred. His relationship to his immediate family and especially to his grandchildren was ideal. He was one of the pediatric pioneers of the Middle West, beloved and respected by all.

J. A. H.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

CAUSES OF THE DESTRUCTION OF CHOLESTEROL IN VITRO. R. P. MACFATE, Am. J. Roentgenol. **18**:151 (Aug.) 1927.

Roentgen irradiation of cholesterol in different solvents shows destruction only with chloroform and carbon tetrachloride. Chloroform and tetrachloride of carbon show increased acidity and oxidizing power on exposure to roentgen rays. The oxy-acids of chlorine, together with chlorine itself, cause the destruction of cholesterol. Hence, the original destruction is due to the probable formation of some oxy-acids of chlorine, strongest in their nascent condition, which are formed by the breaking down of chloroform on irradiation. The reaction is not useful for roentgen measurements which need exclusion of the error of hardness.

STULIK, Chicago.

ANAPHYLACTIC CROSSED RELATIONSHIP BETWEEN HORSE DANDER AND HORSE SERUM. BRET RATNER and HELEN LEE GRUEHL, Arch. Path. **8**:635 (Oct.) 1929.

In a group of ninety-six guinea-pigs sensitized to horse serum, fifteen reacted anaphylactically to dander extract; there were two deaths. When the animals of another series were sensitized to dander extract it seemed much easier to produce a cross reaction with horse serum, fourteen of eighteen reacting; there were seven deaths. Diphtheria antitoxin likewise produced an anaphylactic reaction in these cases. In another group, sensitization was produced by the inhalation of dry horse dander. It is suggested that this mechanism of sensitization is related to the problem of hypersensitiveness of man to horse serum.

LESLIE, Evanston, Ill.

ACID PRODUCTION IN MEDIA CONTAINING CARBOHYDRATES BY GRAM-NEGATIVE INTESTINAL BACILLI. MACKENZIE DOUGLAS, J. Trop. Med. **32**:73 (March 15) 1929.

The action of different organisms on sugars has been made use of in the classification of intestinal bacilli. When bacteria act on carbohydrates they produce acid, acid and gas, or neither. To determine the acidity produced, the p_H is measured by the "capillator" modification of the colorimetric method. The author shows by experiment that acid production in dextrose peptone water is independent of the number of organisms placed in the medium to start with, if sufficient time is given for the organisms to multiply. A maximum is reached, so that the production of acid will come to a constant figure for that organism. Dextrose in a concentration of at least 0.35 per cent is required to enable the organism to produce the maximum acidity.

Peptone and common salt, when used in the medium, exert a buffer action, which tends to prevent a great rise in the p_H.

KANTOR-AMTMAN, Chicago.

THE HYDROGEN ION CONCENTRATION IN MEDIA CONTAINING CARBOHYDRATES BY GRAM-NEGATIVE INTESTINAL BACILLI. MACKENZIE DOUGLAS, J. Trop. Med. **32**:89 (April 1) 1929.

Experiments to determine the effect of the commoner intestinal bacilli on the p_H value of the mediums containing dextrose or other sugars, showed that in those where acid, or acid and gas was produced, the maximum acidity was obtained. Organisms which quickly produced the maximum acidity in dextrose peptone water, were dead in a few days. The same organisms, if grown in sugar-free

peptone water in which acid is not produced, may live for months. *Bacillus faecalis-alkaligenes* does not produce acid in dextrose. Consequently it lives for a long time. It is obvious, therefore, that the production of acid was closely related to the death of the organism.

KANTOR-AMTMAN, Chicago.

THE BACTERICIDAL EFFECT PRODUCED BY THE GROWTH OF INTESTINAL BACILLI IN PEPTONE WATER CONTAINING DEXTROSE AND OTHER SUGARS. MACKENZIE DOUGLAS, J. Trop. Med. **32**:101 (April 15) 1929.

Experiments were made to show the length of life of better known pathologic organisms when grown on different sugars, as influenced by the acid produced. The close association between the death of the organism and the production of acid is again brought out. Dextrose peptone water was inoculated with *Bacillus coli-communior*, and left to incubate until the solution was sterile, when the p_H was 4.2. The fluid was then inoculated with the same organism, which lived for a few days. After each successive inoculation, the fluid became sterile in a shorter period, until the organism died in about forty-eight hours. The resulting fluid treated in this manner will kill a full agar slope of *B. coli-communior* in twenty-four hours. Experiments with other organisms showed that this bactericidal action was not specific. Boiling and filtering do not alter the bactericidal property of this fluid. It is harmless when taken internally. Attempts at therapeutic application have not, as yet, met with much success.

KANTOR-AMTMAN, Chicago.

THE PHYSIOLOGY OF PUBERTY: THE CHANGE IN THE CHEMICAL REACTION OF THE VAGINAL SECRETION. GERTRUD SOEKEN, Ztschr. f. Kinderh. **47**:27 (Jan. 28) 1929.

In 116 girls, from the age of 1 to 15 years old, the hydrogen ion concentration of the vaginal secretion was determined by Soeken; when the organisms were bacilli she found a p_H of 4.3, and when the organisms were cocci, a p_H of 6. A flora of cocci and a weakly acid reaction could always be demonstrated in girls from 1 to 10 years of age; beyond the tenth year, bacillary flora and strongly acid reactions occurred but only in such girls as had already shown signs of puberty. It was to be expected from these researches that the change of flora and of reaction would occur simultaneously and at the beginning of puberty. In one child, by continuous examinations Soeken could observe this change which occurred suddenly within ten days.

EMERSON, Boston.

Nutrition

THE CLEAVAGE OF CARBOHYDRATES BY BACTERIA. MACKENZIE DOUGLAS, J. Trop. Med. **32**:57 (March 1) 1929.

The cleavage of carbohydrates and allied substances is produced by bacteria through their enzyme actions. The author points out the so-called symbiotic fermentation phenomenon, which consists of the combined enzyme action of two organisms neither of which can separately produce the same action. Various enzymes are required to break up the more complex substances, a process which is done in stages, but the accurate steps in the process are not understood—not even the breaking up of dextrose. Most of the complex substances used are broken down to form dextrose or one of the other hexoses, through a process of oxidation, reduction or hydrolysis.

KANTOR-AMTMAN, Chicago.

RICE AND BEANS AS AN ADEQUATE DIET. D. H. COOK and T. RIVERA, Porto Rico J. Pub. Health **5**:16 (Sept.) 1929.

In experiments on rats it was found that while the protein in this diet was fairly adequate and furnished sufficient energy, vitamins B and D were lacking. The mineral content might also fail to be satisfactory.

SANFORD, Chicago.

ALKALOSIS IN A CHILD WITH ENTERITIS. F. HURTADO, Bol. Soc. cubana de pediat. **1**:491 (Sept.) 1929.

Hurtado calls attention to the frequency of a concurrent alkalosis in infants with gastro-intestinal disturbances. As the symptoms are similar to those in toxicosis, alkalis are frequently given by mistake. The author presents the case of an infant, aged 24 months, who was believed to be toxic from a gastro-intestinal disturbance. Examination of the blood showed plasma chlorides to be 2.93 and total chlorides 2.40. It was then found that the child had had convulsions and had been given alkaline therapy. Treatment consisted of transfusion.

SANFORD, Chicago.

NUTRITIONAL DISTURBANCES IN CHILDREN. E. MAIER, Arch. f. Kinderh. **87**: 31 (April 19) 1929.

The author reports on the number of nutritional disturbances in the children's clinic in Freiburg from 1926 to 1927. Of 512 children, 38 per cent were normal, 46 per cent suffered from dystrophy, 6 per cent from over-fat feeding, 6 per cent from prematurity and 2 per cent from various other conditions. Of the cases of dystrophy without infection, 25 per cent were from a deficiency in dextrose, and 17 per cent from strong milk mixtures. In the group caused by infection, 20 per cent were alimentary and 14 per cent parenteral.

SANFORD, Chicago.

FAT-SOLUBLE VITAMIN IN SCHOOL CHILDREN'S DIETS. E. P. WIDMARK and B. SVENSSEN, Skandin. Arch. f. Physiol. **54**:127, 1928.

From the beginning of February to the middle of June, an investigation was carried out on 1,674 school children of both sexes, from the age of 7 to 14 years. Fat-soluble vitamin was given in such a form that the caloric value of the diet was not increased, and observations were made on the weight, height, hemoglobin content of the blood, vision at night, condition of the teeth and incidence of illness. No appreciable difference was found between experimental and control groups except that illness was less frequent in the former. The results show that there is no deficiency in fat-soluble vitamins in the normal diet of school children in Malmo.

KUGELMASS, New York.

EXPERIENCES WITH IRRADIATED ERGOSTEROL. L. VON EORY, Monatschr. f. Kinderh. **45**:50 (Sept.) 1929.

In a child, aged 4, three tablets of irradiated ergosterol daily caused urticaria on the ninth day. The symptoms ceased with discontinuance of the drug and appeared again when the drug was reordered.

In roentgen studies it was shown that irradiated ergosterol increases the tone of a flaccid stomach but has no effect when the musculature is normal. In one case the increased tonus was sufficient to cause vomiting.

GERSTLEY, Chicago.

THREE CASES OF INJURY FROM IRRADIATED ERGOSTEROL. C. WIENER, Monatschr. f. Kinderh. **45**:53 (Sept.) 1929.

The author reports three cases in which small doses of irradiated ergosterol were followed by signs of toxemia, pyelitis and nephritis. The symptoms disappeared with discontinuance of the drug. In one case, the blood calcium was determined and found to be 11.2 mg. Two roentgenograms of the bones of this patient are shown, pictures which the author interprets as showing hypercalcification. While he does not question the value of the drug, he believes that great caution should be shown in the dosage. One of the infants developed symptoms at the end of a week on 5 mg. a day.

GERSTLEY, Chicago.

GENERAL CELL DEGENERATION AS A RESULT OF VITAMIN A DEFICIENCY: COD LIVER OIL IN LARGE DOSES. P. HENRIKSEN, Acta paediat. **8**:397 (June 12) 1929.

Certain forms of cellular injury are sufficiently severe to cause destruction of the cells. Milder forms of injury may lead to a regressive change by virtue of which the cell loses its specific differentiation—into nerve, cardiac tissue, etc.—and resumes the protoplasmic stage. The products of such change are called protoplasts, and may result from a variety of disturbances; the author is particularly interested in their appearance in vitamin deficiency and excessive vitamin dosage. Removal of the source of injury at an appropriate time may lead the cell to resume its characteristic differentiation. Such changes, being common to practically all kinds of cells, warrant a study of all the types of tissue involved rather than of single organs. The changes in the heart which Agduhr reported, for example, as occurring in mice that were fed for a long time on excessively high doses of cod liver oil, do not represent, as has been claimed, a replacement of cardiac muscle tissue by connective tissue but rather regressive changes whereby cardiac cells undergo transformation into protoplasts still capable, if the injury is removed in time, of redifferentiating back into normally functioning cardiac muscle. Moreover, Henriksen claims that such changes are not limited to cardiac muscle but may be found in skeletal muscle and in fact in all differentiated tissues.

Rats were placed on a diet deficient in vitamin A. Six animals were examined after growth had ceased; in all of them, general cell degeneration was found in all the organs. The rest of the rats were then given varying doses of cod liver oil, and the recovery from injury was studied by killing animals at appropriate intervals during the period of ensuing improvement. Degenerated and permanently injured cells were resorbed, while those which had suffered only a regressive change tended to resume their normal appearance and function. One feature of the degenerative process borne out by quantitative studies was the loss of water and the gain of fat content of the brain during the period of vitamin A deficiency.

Another group of rats placed on a diet in which the quantity of vitamin A was diminished but not entirely absent showed a predominance of regressive, rather than degenerative, changes. Many protoplasts were found, and cell division was in abeyance. Histologic studies included the peripheral nerve tissue, brain, spinal cord, skeletal and cardiac muscle, bone, liver, kidney, suprarenal gland and testis.

In a third group of rats, cod liver oil was given in large doses, more than 1.4 Gm. per kilogram of body weight. Here the injury effected an increase, rather than a decrease, in the water content of the tissues so that toward the end there was generalized edema. There was loss of nuclear staining. Protoplasts appeared, just as in the experiments on vitamin deficiency; and again, with appropriate withdrawal of the injury, redifferentiation of protoplasts into functional tissue occurred.

The article is illustrated with drawings, roentgenograms and photomicrographs.

McINTOSH, Baltimore.

INJURY CAUSED BY ANTIRACHITIC AGENTS, WITH PARTICULAR REFERENCE TO THE HEART. C. W. HERLITZ, I. JUNDELL and F. WAHLGREN, Acta paediat. **8**:443 (June 12) 1929.

Mice were used as the experimental animal and were put on the various diets at an age of about 24 to 30 days and a weight of from 7 to 10 Gm. They were killed at intervals of a few months to a little more than a year in some cases, and the hearts were subjected to histologic study. The changes in the cardiac tissue which the authors were looking for were those such as have been described by various investigators as occurring after the prolonged administration of large doses of antirachitic agents: regressive changes in the heart muscle cells; increase in connective tissue; perivascular infiltration; abnormal deposited calcium salts. In the original article, some attempt has been made to estimate quantitative

results. The scope of the investigation is wide, and may perhaps be best presented in the accompanying table.

Injury Caused by Antirachitic Agents in Mice

Series	Diet	Additional Therapy per Mouse per Day	Number of Mice	Number Showing "Marked Changes"	Number Showing Pathologic Calcification	Average Duration of Experiment When Most Marked Changes Were Found
A	Milk, bread, oats	None	10	0	0	—
		0.1 cc. cod liver oil	15	2	2	10½ mos.
		0.002 mg. irradiated ergosterol	15	4	1	11 mos.
B	Water, bread, egg yolk, yeast, lemon juice, McCollum's salt mixture	None	15	1	1	11 mos.
		0.1 cc. cod liver oil	15	4	3	10 mos.
		0.002 mg. irradiated ergosterol	15	1	1	9 mos.
C	Same as series B, with 0.02 Gm. extra yeast	None	10	0	0	—
		0.1 cc. cod liver oil	10	1	1	13 mos.
		0.002 mg. irradiated ergosterol	10	6	3	8 mos.
D	Same as series B, with 0.02 Gm. extra lemon juice	None	10	1	0	11 mos.
		0.1 cc. cod liver oil	10	4	2	10½ mos.
		0.002 mg. irradiated ergosterol	10	6	4	8½ mos.
E	Same as series A	1 drop oil of sesame	10	0	0	—
	Same as series B	1 drop oil of sesame	10	0	0	—
F	Same as series A	0.003 mg. unirradiated ergosterol	5	0	0	—
		0.006 mg. unirradiated ergosterol	5	0	0	—
		0.003 mg. irradiated ergosterol	5	1	0	6½ mos.
		0.006 mg. irradiated ergosterol	5	2	0	4½ mos.
		None	5	0	0	—
		1 drop oil of sesame	5	0	0	—
G	Same as series A	None	4	0	0	—
		Ultraviolet irradiation	4	3	2	2½ mos.

Thus, the authors have detected in the hearts of mice histologic changes which they regard as characteristic, associated with the oral administration of egg yolk, cod liver oil or irradiated ergosterol, as well as with direct ultraviolet irradiation of the animal. Photomicrographs illustrate the types of pathologic change described.

McINTOSH, Baltimore.

THE APPEARANCE OF THE ELECTROCARDIOGRAM IN LESIONS OF THE HEART PRODUCED BY COD LIVER OIL TREATMENT. E. AGDUHR and N. STENSTRÖM, Acta paediat. **8**:493 (June 12) 1929.

In this first instalment of 118 pages, the authors present merely the portion of their work which refers to electrocardiographic changes in the mouse; the study of other animals will follow in subsequent publications. They found distinct abnormalities in the electrocardiograms of their control mice; nevertheless, they felt that the changes occurring in mice treated with cod liver oil are sufficiently more frequent and more marked to justify them in drawing conclusions from this technical approach. To the basal diet they added cod liver oil in the following amounts per kilogram per day: 0.01, 1, 3, 5 cc. and a still greater but indefinite quantity administered by soaking the bread of the diet in cod liver oil. Selected electrocardiograms from each group are reproduced and are discussed at considerable length. An increase in conduction time and alteration of the ventricular complex with or without prolongation of the Q R S interval occurred frequently. In the histologic work, not only were regressive and degenerative changes found, of the type previously described by Agduhr in numerous publications, but an attempt was made to evaluate hypertrophy and thus account for deviations of the electrical axis of the heart. The photomicrographs accompanying the article are numerous and unusually clear.

McINTOSH, Baltimore.

THE RELATION OF THE ENDOCRINE ORGANS TO RICKETS AND TETANY. L. STOLTENBERG, Norsk. Mag. f. Lægevidensk, July, 1929, p. 729.

The author produced rickets and tetany in rabbits by giving them a rachitic diet and by excluding sunlight from their cages.

He then studied the pathologic anatomy of the thymus, suprarenal, thyroid and parathyroid glands.

The thymus and suprarenal glands showed no changes that might be related to rickets or tetany.

The thyroid gland showed the same picture as that caused by hyperfunction of the gland: enlargement of the whole gland, and microscopically, a large number of epithelial cells and a small amount of colloid in the alveoli. There was no sign of degeneration.

The parathyroid glands were always enlarged when the animals had been given the diet for several weeks. This enlargement was also considered as hyperplasia on account of the morphology of the cells.

The author considers this hyperplasia of both thyroid and parathyroid glands as a hyperfunction of both glands and states his belief that this is one of the ways that the animal reacts to the insufficient diet.

TOVERUD, Oslo, Norway.

RICKETS AND THE ANTIRACHITIC FACTOR. JAN STRITESKY, Časop. lék česk., Dec. 23, 1927, vol. 66, no. 52.

The author reviews the entire literature on rickets and takes up the studies on etiology, the relation of calcium and phosphorus, sunlight reaction, attempts at isolation of vitamin D, ultraviolet therapy and ergosterol. He brings out the fact that the antirachitic factor is destroyed through periods of irradiation longer than seventeen hours. He regards ergosterol as a provitamin, since its activation produces vitamin D.

STULIK, Chicago.

THE NUTRITIVE DEVELOPMENT OF AN INFANT FED EIGHT MONTHS ON A SOY BEAN DIET. ERNEST TSO, Chinese J. Physiol. **2**:33, 1929.

An infant, aged 6 weeks, was fed on soy bean "milk" supplemented by cane sugar, cod liver oil, orange juice, egg, rice porridge, spinach and sodium chloride. Rickets appeared, but disappeared after the calcium ration was increased. The child grew 20.7 cm. and gained 4.1 Kg. in weight in eight weeks.

KUGELMASS, New York.

GROWTH OF RATS ON VEGETARIAN DIETS. H. WU and D. Y. WU, Chinese J. Physiol. **2**:173, 1929.

Young rats fed on cereals, pulses and various Chinese vegetables grew, in some cases, about one-half as fast as those fed on wheat and milk powder. Diets containing "small cabbage," colza, Kan Lan Ts'ai or Kai Ts'ai were more satisfactory than others; the growth of the first generation was normal, but the next generation was undersized.

KUGELMASS, New York.

Prenatal Conditions

CASE OF VOLVULUS OF THE STOMACH WITH CONGENITAL ANOMALIES OF DEVELOPMENT. J. A. GORRELL, Canad. M. A. J. **21**:427 (Oct. 23) 1929.

A male breast-fed infant, aged 10 months, suddenly developed severe pain and later vomited.

Operation revealed a greatly dilated stomach which had been rotated from right to left on a vertical axis passing through the cardiac orifice. The duodenum was wound one complete turn around the pyloric orifice, causing complete pyloric obstruction. The patient lived for fourteen hours after the operation.

Postmortem examination showed the great omentum to be about 1 inch long; it did not contain the transverse colon. The gastrohepatic omentum was about 5 inches long and allowed the stomach to be very mobile. Other anomalies were present.

MOORE, Omaha.

ENDOCRINE AND OTHER ANOMALIES IN ANENCEPHALY. G. H. ETTINGER and JAMES MILLER, J. Obst. & Gynec. Brit. Emp. **36**:552, 1929.

In anencephalic monsters the only consistent endocrine anomalies accompanying the absence of the pineal gland are in the suprarenal gland and pituitary body. The former, usually present, exhibits a precocious or postnatal state of development but may be absent. The pituitary body is almost always present but rarely shows nervous elements. It is conjectural as to whether these endocrine defects cause or follow the cephalic and general condition. The absence of the pars nervosa and the presence of a well developed retina point toward a destructive process and indicate such a factor in the causation of the anencephaly.

If the fetal suprarenal cortex were concerned with the elaboration of brain lipoids, a destruction of the brain might result in a disuse atrophy of the former. A defective pituitary gland and absence of the pineal gland might be responsible for skeletal and visceral defects and anomalies. Experimental destruction of fetal brain might settle the question. The authors describe two cases with fluid accumulation between the kidney and its capsule with aplasia of suprarenal glands in both.

ADAIR, Chicago.

CRANIO-CLEIDO-DYSOSTOSIS. ERIC A. CROOK, Proc. Roy. Soc. Med. **22**:1243 (July) 1929.

A case of cranio-cleido-dysostosis was reported in a girl, aged 8. On routine examination, the patient was discovered to have both clavicles divided in the middle. The outer half of the bone is the part which most frequently shows variation and is often absent in cases of cranio-cleido-dysostosis.

WILLIAMSON, New Orleans.

THE FUTURE OF PREMATURE INFANTS. OSCAR HERZ, Monatschr. f. Kinderh. **45**:1 (Sept.) 1929.

The term "premature" has been used clinically to describe any infant with a birth weight under 2,500 Gm. This is not correct, technically, because many children that are born at full term weigh only 2,500 Gm., due to illness of the mother. The term premature should be used with more caution than it has been in the past.

The author reviews the literature carefully and includes 252 cases of his own. Of these he excludes 57, as a carefully taken history made it doubtful that they were true premature infants. The highest mortality occurs on the first day, and the most frequent cause of death is intracranial hemorrhage. The diagnosis of death due to prematurity alone should never be made.

Other causes of death were bronchopneumonia and apnea. The attacks of apnea, except those occurring in the first days, were usually secondary to other conditions.

The mortality of the illegitimate children born in the hospital was no greater than that of the legitimate.

The author was unable to find any definite symptom that was suggestive of injury at birth. Unquestionably the development of many attacks of apnea was due to this cause. Craniotabes appears in all premature infants. The localization depends on the position of the child and appears first on the side that is habitually turned to the bed.

Premature infants tend to develop pigmented skin; they are predisposed to umbilical and inguinal hernias, to anemia, to exudative diathesis and to infections.

In the author's series, from 4 to 6 per cent of infants showed defective mental development.

GERSTLEY, Chicago.

CYSTS AT THE BASE OF THE TONGUE IN CONGENITAL STRIDOR. E. THOMAS, Ztschr. f. Kinderh. **47**:168 (Jan. 28) 1929.

Thomas approves the advice by Post to make a careful palpation of the throat in every case of congenital stridor. Before total extirpation of such a tumor, however, it is better to make sure that the thyroid gland is present in its usual place, lest with the removal of the tumor everything of thyroid nature that the child has is taken away (so-called dystrophia hypoplasia of the thyroid). After a time such conditions become myxedematous. Numerous cases of this sort have been described, a part of which are in the monograph, Internal Secretions in the Early Years of Life. It may be necessary even to make an exploratory incision if by palpation alone one cannot be sure that the thyroid is present.

EMERSON, Boston.

Diseases of the New-Born

SPONTANEOUSLY HEALED SEPSIS WITH STAPHYLOCOCCI IN AN INFANT AGED EIGHT WEEKS. E. BAHL, Ztschr. f. Kinderh. **47**:166 (Jan. 28) 1929.

Bahl reports a spontaneously healed sepsis with staphylococci in an infant, aged 8 weeks, who showed a positive blood culture. The portal of entrance was probably pharyngitis. Nothing was done therapeutically.

EMERSON, Boston.

Acute Infections

DIAGNOSTIC VALUE OF THE VACCINIA VARIOLA FLOCCULATION TEST. W. L. BURGESS, JAMES CRAIGIE and W. J. TULLOCH, Medical Research Council, sp. ser. bull. 143, 1929.

The authors examined ninety-six specimens of crusts from ninety-three cases of smallpox, chickenpox, vaccinia and other conditons and found that the vaccinia flocculation test gave reactions of diagnostic value. As the material was from many varied sources, they do not believe that it could be due to invading organisms. To test this further, the vaccinia serum was absorbed with staphylococci obtained from vaccinnia crusts, and tested with extracts from the same crusts. The authors state their belief that the reaction is due to the union of the antigen with true antibodies to the virus.

SANFORD, Chicago.

EXPERIMENTAL MEASLES IN MONKEYS. P. M. OTERO and E. B. MCKINLEY, Porto Rico J. Pub. Health **5**:36 (Sept.) 1929.

The authors were unable to find any organism in cultures made in six cases of measles. Monkeys which were given injections of blood from these patients developed measles, but the cultures were negative. The authors believe that their failure to find streptococcus in measles occurring in human beings and in monkeys is direct evidence against the streptococcus etiology of measles. In the tropics, streptococcus infections are not as common as in temperate climates; hence as measles is common in the tropics, it is of doubtful value to assign to this organism the etiologic rôle in the disease.

SANFORD, Chicago.

TOPOGRAPHY AND PATHOGENESIS OF LESIONS IN RHEUMATIC FEVER. A. F. BERNARD SHAW, Arch. Dis. Childhood **4**:155 (Aug.) 1929.

Cardiac lesions are merely local manifestations of a general infection. The postmortem examination of a girl, aged 15 years, is reported. Excellent illustrations are submitted of the Aschoff nodes, which were found distributed throughout the body. The studies indicate that rheumatic endocarditis is embolic in origin. Valvulitis precedes endocarditis, and the latter cannot develop until the inflammatory process has permeated the leaflet as far as the line of closure.

PETERMAN, Milwaukee.

PAROXYSMAL SNEEZING IN WHOOPING COUGH. ALAN MONCRIEFF and R. C. LIGHTWOOD, Arch. Dis. Childhood **4**:240 (Aug.) 1929.

A case is reported in a child, aged 3 years and 11 months. The paroxysmal sneezes followed the characteristic whooping. Bacteriologic examination of the nasal discharge demonstrated organisms of the pertussis type.

PETERMAN, Milwaukee.

POSTDIPHTHERITIC HEMIPLEGIA. C. WORSTER-DROUGHT and I. M. ALLEN, Proc. Roy. Soc. Med. **22**:640 (March) 1929.

A girl, aged 9 years, had had a severe attack of diphtheria at the age of 4, and on discharge from the hospital her legs were weak. A few weeks later, the left leg had recovered and it was noticed that the patient limped with the right leg. The arm became affected later. At the time she was seen by the author, she was unable to use the right arm and leg; this was five years after the attack of diphtheria. The previous and family history and condition found on examination are given in the report.

Hemiplegia as a complication of diphtheria occurs somewhat rarely. It is vascular in origin and due to embolism, thrombosis or hemorrhage.

WILLIAMSON, New Orleans.

EXANTHEM SUBITUM. TEITEL, Arch. de méd. d. enf. **32**:327, 1929.

This disease of early childhood, resembling measles in many respects, has three essential features (*a*) a sudden rise of temperature without prodromal symptoms; (*b*) a morbilliform eruption appearing immediately after the febrile attack, and (*c*) disappearance of the eruption without desquamation or pigmentation.

The first description of the disease was made by Zahorsky, in 1913, under the name roseola infantum; in 1921, Veeder and Hempleman reported twenty cases and gave to the disorder the present name of exanthem subitum. Teitel reviews the literature of the disease from that period, particularly the reports of observers in Japan, Russia, Hungary and America; up to the present time about 200 cases have been reported. Although it may be considered as an infection it is not readily communicable, and there is no instance of direct transmission from one child to another, even in the same family. It is practically confined to the first two years of life, although American clinicians have reported one case in a child, aged 10, and in another, aged 14. The onset is brusque; the temperature rapidly rises to 103 or 104 F., while the constitutional symptoms may be unimportant; there may be slight congestion of the pharynx but no cough, nasal catarrh or conjunctivitis; Koplik's spots are absent and the urine is negative. The heart sounds are normal, and the liver and spleen not palpable. Usually on the fourth but occasionally on the fifth or even the sixth day there is a sharp fall in temperature, followed in about twenty-four hours with a measles-like eruption most commonly on the back and from this area gradually spreading to the abdomen and the extremities. It is practically negligible on the face. After a day or so this rash disappears without a trace of desquamation or staining of the skin. In certain cases a second rise of temperature has been noted but this is always of short duration. An interesting clinical manifestation of this exanthem is the leukopenia, which may be as low as 3,000, and the presence of marked lymphocytosis. The blood picture therefore provides a diagnostic clue of exceptional importance. Careful consideration of the natural history outlined should make the differential diagnosis relatively easy. In his work in Palestine, Teitel observed nine cases which he describes in detail.

AMESSE, Denver.

PEMPHIGOID VARICELLA. P. GAUTIER and A. THÉVÉNOT, Rev. franç. de pédiat. **5**:363 (June) 1929.

The authors report a case of varicella which, after a few days, presented the appearance of pemphigus. The child was in the hospital, and the transformation

of the lesions from the typical vesicles of varicella to large irregular bullae could be observed. The latter resembled burns about 5 cm. in diameter. The fluid from the lesions was sterile. The question of a pemphigus complicating the varicella was raised, but the gradual development of the lesions and the fact that no other cases were observed argues against this. The article is illustrated.

LESLIE, Evanston, Ill.

VARIOLOID COMPLICATED BY EMPYEMA. MARTINEZ VARGAS, Med. de los niños **30**:210 (July) 1929.

A boy, aged 3 years, became ill with varioloid, the usual prodromal symptoms being followed on the second day by an intense pustular eruption. Three days later, generalized pain, dyspnea and signs of pleural effusion appeared. After the eruption disappeared, an intercostal drainage was performed and staphylococcus was found to be the causative organism. The author states that this complication is not common.

DWYER, Kansas City, Mo.

THE LEUKOCYTIC INDEX OF KREBS AND THE NUCLEAR INVERSION OF VÉLEZ IN SCARLET FEVER. A. LEONI, Riv. di clin. pediat. **27**:435 (May 30) 1929.

The author has studied the differential white blood cell count and the number of nuclei in the neutrophilic leukocytes in 100 cases of scralet fever.

In the eruptive stage of scarlet fever, the ratio of polymorphonuclear neutrophils to lymphocytes was usually increased; this ratio became normal during the desquamative stage; in one fatal case, the ratio became subnormal just before death. In normal children, the ratio was 1:1; in mild cases of scarlet fever it was usually 7.5:1, and in severe cases usually about 20:1 (maximum, 60:1).

The number of polymorphonuclear neutrophilic cells with one and two nuclear bodies was markedly increased during the eruptive stage of severe scarlet fever; the unusual observation of only one nuclear body in the majority of these cells occurred in several severe cases.

These observations are believed by the author to be useful in the prognosis of scarlet fever.

HIGGINS, Boston.

DOUBLE INFECTIONS IN CHILDREN. F. L. PRESTI-SEMINARIO, Riv. di Clin. pediat. **27**:483 (May 30) 1929.

The author quotes from the literature and his own experience the reports of cases in which children have had more than one infectious disease at the same time. He divides them into three groups: (*a*) two bacterial diseases, (*b*) a bacterial and a parasitic disease and (*c*) two parasitic diseases.

HIGGINS, Boston.

PLASMOCHIN THERAPY IN THE MALARIA OF CHILDREN. B. DE LUCA, Riv. di clin. pediat. **27**:501 (May 30) 1929.

Plasmochin is a synthetic derivative of quinoline and is used in the treatment of malaria. It is not as bitter as quinine, and children take it voluntarily. The author reports nine cases in which it was efficacious. He recommends its use also as a prophylactic measure against malaria.

HIGGINS, Boston.

SERUM THERAPY IN POSTDIPHTHERITIC PARALYSIS. A. VENUTI, Riv. di clin. pediat. **27**:522 (May 30) 1929.

The author reports ten cases of postdiphtheritic paralysis, in six of which he gave diphtheria antitoxin. He does not believe that the giving of antitoxin even in the severe cases is of any therapeutic value. However, he experienced no untoward effects of the serum, even when manifestations of anaphylaxis were present.

HIGGINS, Boston.

ENCEPHALOMYELITIS AND JENNERIAN VACCINATION. B. BENVENUTI, Riv. di clin. pediat. **27**:580, 1929.

A child, aged 25 months, on the tenth day following vaccination developed a high fever, headache, chronic and tonic convulsions, enlarged pupils, stupor and slight rigidity of the neck. Twenty days later, she had recovered completely.

A review of the literature shows that about 50 per cent of the reported cases of vaccinial encephalitis have proved fatal.

HIGGINS, Boston.

A NEW SYMPTOM OF MEASLES: THE HEMORRHAGIC PREEXANTHEM. GEZA PETENYI, Monatschr. f. Kinderh. **45**:61 (Sept.) 1929.

In the prodromal stage of measles, punctiform hemorrhages appear on the mucous membrane. On the cheeks they occupy the site on which Koplik's spots develop later; they are also present on the soft palate. The number on the cheeks is somewhat smaller than that on the soft palate, being from about three to eight on the former and as high as twenty on the latter.

The spots appear from one to three days before Koplik's spots and last from two to three days. At this time, the mucous membrane of the mouth is not injected, so that these punctiform hemorrhages are sharply demarcated. They appear in six of fourteen cases observed.

GERSTLEY, Chicago.

IDIOPATHIC GLANDULAR FEVER. H. LEHNDORFF, Wien. klin. Wchnschr. **42**:985 (July 25) 1929.

An excellent critical survey is given of what is known about "infectious mononucleosis," which as the author shows is better called idiopathic glandular fever.

CLAUSEN, Rochester, N. Y.

PROPHYLAXIS OF MEASLES WITH REACTIVATED SERUM OF ADULTS. H. BAAR, Wien. klin. Wchnschr. **42**:1140 (Aug. 29) 1929.

This article gives the details of the method already described in the AMERICAN JOURNAL FOR DISEASES OF CHILDREN (**38**:219 [July] 1929). Of seventy-three children exposed to measles who received from 3 to 10 cc. of reactivated serum, eleven developed abortive measles. Of those who received serum obtained from adults who had had two or more vaccinating injections, only one developed measles.

CLAUSEN, Rochester, N. Y.

WHOOPING COUGH AND ENLARGED HEARTS. KLOTZ, Ztschr. f. Kinderh. **46**:818 (Dec. 15) 1928.

Dr. Klotz believes that the smallness of the heart in some infants with acute pertussis may be related to the general loss of weight. Using Lang's apparatus to keep the children still, at a distance of 25 cm., he measured the hearts of twenty-seven children of normal weight, aged from 3 to 5 years, who were ill with the whooping cough. Fifteen had large hearts, three had normal hearts and nine small hearts. In the convulsive state, three of twenty-seven patients remained uninfluenced; in one-third there was diminution of the size of the heart and in one half an increase in size. Thus, Klotz agrees with Chajes as to the patients with large hearts being in the majority and also that there is an increase in size with bronchopneumonia and with serous meningitis. He does not agree that a small heart excludes an infection with fever. He is not certain that either the severity of changes in the thorax due to rickets or the severity of the whooping cough causes an enlargement of the heart, for he found in patients with rickets, without any consistency, hearts that were too large and hearts that were too small. He confirms Feldmann's observation of small hearts in a series of infants with whooping cough, but these can depend on other causes than whooping cough.

While Feldmann found in six acutely sick, small children not one large heart, nevertheless, the hearts that were larger than normal were more frequent than the smaller ones.

EMERSON, Boston.

ACTIVE IMMUNITY WITH TOXIN-ANTITOXIN VII AND TOXIN-ANTITOXIN VI OF VON BEHRING. JAROSLAV PROCHAZKA, Časop. lék. česk. **65**:1234 (Aug. 13) 1926.

All children admitted to the measles and scarlet fever wards were immunized with toxin-antitoxin of von Behring. Children under 18 months received the stronger dilution, VI, and those over 18 months dilution VII. Neither blood titration nor Schick tests were used, but dilutions of 1:39 were used in 0.1 cc. doses. If no reaction resulted in forty-eight hours, a 1:16 dilution was used; and if no reaction occurred in forty-eight hours, a 1:5 solution. Undiluted toxin-antitoxin was given in the final injection if no reaction resulted (a 2 cm. or greater, elevated, red and slightly tender reaction was used as a criterion). After ten days the toxin-antitoxin VII or VI was again injected in the dilution which produced a reaction; 0.1 cc. doses were used throughout.

Toxin-antitoxin VII and VI can be used without danger. Even in the presence of diphtheria no anaphylactic reaction takes place. Immunity results after four weeks in most instances, but some value is obtained during the first weeks—an effect on the severity of the disease and on the death rate. Inoculation is harmless even in those who have had diphtheria, and the immunity acquired lasts over a year and a half. Of 162 children immunized, 14 developed diphtheria before the establishment of immunity, but all had mild cases and not one died.

STULIK, Chicago.

A RECENT EPIDEMIC OF SCARLATINA-LIKE ERUPTIVE FEVER IN KANAZAWA. S. IZUMI, T. YAGASAKI and N. SUGISHITA, J. Pediat. (Tokyo), 1929, no. 347, p. 667, and no. 348, p. 862.

The authors studied ten typical cases of a hitherto unrecognized form of eruptive fever somewhat resembling scarlatina which occurred in an epidemic in 1927 in certain parts of Japan. The rash resembles closely that of scarlet fever, although the clinical course is more like that of German measles. The authors first thought it might be a form of the so-called fourth disease of Dukes-Filatoff, but there were a number of discrepancies. The duration of fever, ranging between 100 and 101 F., was usually from one to two weeks. The rash was multiform, in some cases tending to be localized and appearing morbilliform, while in others it was diffuse with marked erythema of healthy skin. The rash had no tendency to become hemorrhagic, and no vesicle formation was seen. The rash faded usually in three or four days, with desquamation following in two or three weeks without any discoloration of the skin. The white count rose to 27,000 during the febrile period, with an increase in eosinophils. The urine showed a slight amount of albumin with some evidences of acute nephritis which usually cleared up with the fall in temperature. The diazo and urobilin reactions were negative, while the urobilinogen reaction was usually strongly positive. The rash sometimes reappeared during convalescence, with the reappearance of a positive urobilinogen reaction which once became negative with the fall in temperature.

The authors studied the bacteriology of this disease. In two cases, they tested the spinal fluid and in three cases the blood; all the specimens were taken during the height of the fever. The culture medium was a modification of Leventhal's blood-bouillon fluid mediums. In five cases, they obtained a coccus closely resembling *Staphylococcus albus*, which gave a positive reaction to the agglutination test in comparatively high dilutions, becoming negative in dilutions over 3,200 when tested against the immune serums of rabbits, while the control showed a negative reaction in as low a dilution as 200.

The authors do not claim that this coccus is positively related etiologically to the disease in question, as the data are insufficient, but they hope to be able to demonstrate some etiologic relation in future studies.

BACILLI OF A PARA-TYPHOSUS GROUP ISOLATED FROM A CASE OF DYSENTERY. NAOSHI ORIISHI, J. Pediat. (Tokyo), May 20, 1929, no. 348, p. 828.

The author made a careful bacteriologic study of the feces in a case of colitis in a girl, aged 6 years, with all the typical symptoms of dysentery. He could find no trace of *Bacillus dysenteriae,* but succeeded in isolating a variety of *Bacillus paratyphosus.* This microbe resembles closely *B. paratyphosus* X (Mita) in its physical and biologic aspects, but differs in the fact that atypical forms of *B. dysenteriae* can be agglutinated in a remarkable degree by the serum immunized by this bacillus. The author was able to satisfy himself of the etiologic relations of this bacilli by agglutination and complement fixation tests. The toxicity of this bacillus is far greater than that of either *B. dysenteriae* or *B. paradysenteriae,* and approaches that of *B. paratyphosus.* Again, in his second case, he isolated a microbe closely resembling *Bacillus enteritidis* (Goertner), which he identified by the general characteristics and by serologic tests. By oral administration of this bacillus, he produced the death of mice. From these two cases, it may be said that cases of colitis with typical clinical symptoms of dysentery can be caused by a variety of *B. paratyphosus.*

KATO, Los Angeles.

Chronic Infections

FEBRILE BODY TEMPERATURES AS POSSIBLE ADJUNCT TREATMENT IN WASSERMANN-FAST SYPHILITIC PATIENTS. LEE D. CADY and F. H. EWERHARDT, Am. J. Syph. **13**:313 (July) 1929.

The authors have used hydrotherapy to increase the body temperature of patients who have Wassermann-fast syphilis, the temperature being raised from 103 to 107.2 F. Many patients became uncomfortable at 104 F., and two became delirious at 105 and 107.2 F., respectively.

The majority of the patients felt better on the following day. The effect on the Wassermann reaction was not impressive. The studies are being continued.

MCBRIDE, Sioux City, Iowa.

SYPHILITIC HEADACHES. JOSEPH KOPECKY, Am. J. Syph. **13**:332 (July) 1929.

The author noted that a large number of the patients who entered the medical outpatient department came because of pain.

Of 4,300 patients admitted, 882 were syphilitic, and 670 of these gave pain as their chief complaint.

In 71.5 per cent there was no basis for the pain other than syphilis; 131 gave headache as their chief complaint. The author brings out the fact that tertiary syphilis may have been responsible for the headache in 78 of the patients; secondary syphilis, in 36, syphilitic periostitis, in 4; cerebral syphilitic endarteritis, in 4; syphilitic meningitis, in 3; syphilitic aortitis, in 2; cerebrospinal syphilis in 1; gumma of the cranium, in 1; gumma of the lung in 1, and paresis in 1.

He also emphasizes that all patients who complain of headache should have a complete examination including a Wassermann test before being subjected to treatment.

MCBRIDE, Sioux City, Iowa.

PREVIOUS TREATMENT OF PATIENTS WHO HAVE DEVELOPED NEUROSYPHILIS. FRANCIS E. WEATHERBY, Am. J. Syph. **13**:339 (July) 1929.

The author has made a study of the case records of neurosyphilitic patients who have come into the army medical service at the Walter Reed General Hospital with a view of ascertaining the relation of previous treatment to the development of the various types of neurosyphilis. His conclusions are as follows:

1. There is no evidence that treatment with arsphenamine in the early stages of syphilis predisposes to the development of paresis. Paresis usually develops in the undiagnosed, neglected and inadequately treated patients.

2. Arsphenamine appears to predispose to the early onset of cerebrospinal syphilis. However, untreated patients with apparently late onset may have had early cerebrospinal involvement and this might have been discovered if they had been examined in early stages of their infection.

3. The factor of neglect does not appear as prominently in cases of tabes and of psychosis with cerebral syphilis as it does in paresis, but the majority of patients have had no previous treatment.

4. In spite of malaria at various intervals of time after syphilitic infection, paresis and other forms of neurosyphilis can develop.

McBRIDE, Sioux City, Iowa.

EARLY SYPHILIS. LOUIS CHARGIN and ABRAHAM STONE, Arch. Dermat. & Syph. **19**:750 (May) 1929.

The results of treatment of 444 patients with early syphilis are presented. An apparent cure was effected in 60 per cent of the whole group. The greatest number of cures, 90 per cent, was obtained in the primary seronegative group—the patients who came under treatment with a primary lesion and a positive dark-field, and a negative Wassermann reaction. In both the primary seropositive and early secondary groups, the percentage of probable cures was 61 per cent. Delay of treatment beyond the third or fourth month reduced the number of cures to 45 per cent. Several methods of treatment were used. The best results were apparently obtained with the intensive plan of treatment, the aim of which is to saturate the patient with the arsenical preparation at the beginning of each course of treatment.

SHIRLEY, Iowa City.

THE THERAPEUTIC ACTION OF COLLOIDAL MERCURY SULPHIDE AND OF OTHER COLLOIDAL HEAVY METAL SULPHIDES IN SYPHILIS EXPERIMENTALLY PRODUCED IN RABBITS. G. EARLE WAKERLIN, Arch. Dermat. & Syph. **19**:879 (June) 1929.

Colloidal mercury sulphide, in doses of one tenth of the maximum tolerated dose, was found to possess excellent healing and definite sterilizing properties in the rabbit experimentally infected with syphilis, and its potency was proved superior to that of other known mercurials. Colloidal bismuth sulphide, in a range of one half of its maximum tolerated dose, is an effective healing agent but an ineffective sterilizing agent, and is inferior to potassium bismuth tartrate. Colloidal copper sulphide, in doses of one tenth the maximum tolerated dose, was devoid of therapeutic activity. All of the colloids investigated were without deleterious effects on the tissue at the site of intravenous administration, and were apparently free from the properties responsible for the production of anaphylaxis in rabbits.

SHIRLEY, Iowa City.

RETENTION OF BISMUTH IN THE ORGANISM IN THE TREATMENT OF SYPHILIS. SVEND LOMHOLT, Arch. Dermat. & Syph. **19**:891 (June) 1929.

The fate of bismuth oxychloride, in weak concentration (about 1 per cent) but in large doses, injected intramuscularly into the hind legs of guinea-pigs was investigated. It was concluded that the major part of the quantity injected was excreted relatively quickly with the urine and feces. From seven to ten days later, only from 4.7 to 13.1 per cent was left. A portion of this remained at the site of injection. Of the remainder in the body, the major part was deposited in the abdominal viscera, especially the kidneys, liver and large intestine. In other parts of the body, relatively small quantities were found.

SHIRLEY, Iowa City.

LOCAL MICROSCOPIC CHANGES FOLLOWING THE ADMINISTRATION OF ANTISYPHILITIC DRUGS. O. M. GRUHZIT, Arch. Dermat. & Syph. **19**:922 (June) 1929.

The pathologic changes induced by the intramuscular injection of arsenic, mercury and bismuth are studied. The arsphenamine type of drugs administered intramuscularly invariably causes tissue necrosis with the formation of a sterile abscess which heals slowly. Sulpharsphenamine causes as much injury as neosulpharsphenamine. Mercury compounds produce the same type of injury, but to a less degree. Bismuth compounds cause local injury depending on the degree of the corrosiveness. The least injurious bismuth preparations are the water-soluble, tissue fluid soluble compounds, such as bismuth thioglycollate.

SHIRLEY, Iowa City.

THE SPIROCHETICIDAL ACTIVITY OF THE HUMAN SYPHILITIC SERUM AND THE IMMUNOLOGIC SIGNIFICANCE OF THE WASSERMANN REACTION. JOHN A. KOLMER and ANNA M. RULE, Arch. Dermat. & Syph. **20**:90 (July) 1929.

Serum from patients with active and latent cases of syphilis and giving positive Wassermann reactions were no more spirocheticidal in vitro, produced no more curative effects in rabbits with syphilis produced by inoculation, and had no more prophylactic activity in rabbits than serum from nonsyphilitic persons. The author therefore concludes that no part of acquired immunity in syphilis is humoral, that the Wassermann antibody is not spirocheticidal but may be an index of tissue immunity, and that serum prophylaxis and treatment for syphilis is not possible by present methods.

SHIRLEY, Iowa City.

EXPERIMENTAL STUDIES ON CALMETTE'S B.C.G. VACCINE. W. LITTERER, South. M. J. **22**:955 (Nov.) 1929.

From experiments with B.C.G. vaccine variously given to guinea-pigs and subcutaneously inoculated into human beings, the author is convinced of its innocuousness and its harmlessness, especially if Calmette's technic be rigidly followed.

Subcutaneous inoculations of the B.C.G. vaccine were given to eighty-six persons ranging in age from 1 to 50. Ninety per cent of these developed tuberculin allergy in eight weeks.

The majority of patients receiving 0.01 mg. of the vaccine subcutaneously developed cold abscesses. The abscesses produced little or no discomfort and healed readily when opened. Tuberculin allergy was produced in every case of abscess formation.

Immunity could be obtained in abscess formation by lessening the dosage of the vaccine.

The preferred method of administration of B.C.G. vaccine is subcutaneously, as it is more definite and reliable and has a wide range of applicability.

Oral administration is less reliable for new-born infants, and should later be supplemented by subcutaneous inoculations.

SCHLUTZ, Minneapolis.

A CASE OF PROBABLE ANTENATAL TUBERCULOUS INFECTION. R. H. MORLEY, Arch. Dis. Childhood **4**:227 (Aug.) 1929.

Miliary tuberculosis was demonstrated post mortem in an infant, aged 6 weeks. The lesions in the liver and celiac glands were considered to be of more than six weeks' duration. This evidence is taken to suggest a direct infection from the placenta. No tuberculosis was demonstrated in the mother or in the relatives. This case probably belongs with many of the other reported cases of congenital tuberculosis which have not been proved.

PETERMAN, Milwaukee.

ALBUMIN IN THE SPUTUM AS AN AID TO THE EARLY DIAGNOSIS OF PULMONARY TUBERCULOSIS. PERCY MOXEY, Practitioner **123**:142 (Aug.) 1929.

A report is given of the examination of sputum in early cases of tuberculosis or in cases in which the condition is thought to exist. Moxey points out that sputum does not always show tubercle bacilli in the early stages.

It has been shown that albumin is almost constantly present in the sputum in pneumonia, pulmonary edema and pulmonary tuberculosis.

In a series of over 2,500 examinations of sputum for the presence of both tubercle bacilli and albumin it was found that a close relationship exists between the quantity of albumin and the number of bacilli present. In the author's series, in which five or fewer bacilli were present for fields of ten on a slide, the albumin was 0.06 per cent; when twenty bacilli were found, the albumin increased to 0.09 per cent, and when fifty bacilli were found, the albumin was found to be 0.1 per cent.

In the 2,500 examinations of sputum, 25 per cent showed both bacilli and albumin; in nearly 50 per cent, albumin only was found, and in the remaining number, neither albumin nor bacilli. The author states that during a four years' investigation there were only two cases examined in which bacilli were found and no albumin, and that in both these cases albumin was found on carrying out a second test.

The method of quantitative examination of the sputum is as follows: To 10 cc. of the sputum 30 cc. of 1 per cent acetic acid is added and shaken until thoroughly mixed. This causes precipitation of mucus. The mixture is filtered through filter paper. The filtrate is tested for albumin qualitatively and quantitatively (Esbach's method for the latter).

Moxey concludes that the presence of albumin in the sputum in the absence of pneumonia or pulmonary edema is strong evidence of a pulmonary lesion and when such observations are made, even though bacilli have not been demonstrated, treatment should be started at once.

SAPPINGTON, San Francisco.

THE SYNDROME OF CAVITY FORMATION IN THE INFANT. T. VALLEDOR, Bol. Soc. Cubana de pediat. **1**:442 (Aug.) 1929.

The author reports ten cases in full with roentgenograms and laboratory data. He concludes that the origin of the tuberculous cavity is necrotic caseation from a primary focus. The bronchopneumonia tuberculous form comes on much later. The number, form and size of the cavities vary with individual conditions. Clinically there is no special sign that might lead to the diagnosis; complete exploration roentgenically and by fluoroscopy is the only satisfactory method. Among the complications the most frequent is pneumothorax.

SANFORD, Chicago.

TUBERCULOUS MENINGITIS WITHOUT TUBERCLES. MARTINEZ VARGAS, Med. de los niños **30**:209 (July) 1929.

A girl, aged 4 years, became ill ten days before entering the hospital; she showed loss of appetite, exhaustion and pains in the head. Under observation in the hospital she was stuporous much of the time, with convulsions, opisthotonous, hydrocephalic cry, a positive Kernig sign, vomiting without nausea, dilated and unequal pupils, desiccation of the cornea and bilateral divergent strabismus. The spinal fluid was under pressure, the cell count 40 with a predominance of lymphocytes; no organisms were found. The Pirquet reaction was positive and the Wassermann negative.

Necropsy revealed a hyperemic meninges with numerous adhesions to the cerebrum. The cerebral mass was soft and edematous, the frontal and parietal lobes were very friable and zones of ecchymosis were found throughout the white matter. The author did not observe macroscopically, any tubercles of the meninges or the nerve tissue after close inspection. Aside from the emaciation and enlarged bronchial glands there were no other positive observations.

DWYER, Kansas City, Mo.

THE PIRQUET REACTION: A COMPARISON OF VARIOUS DILUTIONS. D. FABIAN ISMAT VILA, Med. de los niños **30**:211 (July) 1929.

Three dilutions of Koch's old tuberculin were used to study the intensity of the reaction in the different types of tuberculosis. Dilutions of 1:10, 1:20 and 1:30 were used. In hundreds of cases it was found of value in studying the form and grade of the lesion.

Lesions of the serous membranes, pleura, pericardium and meninges gave a definite reaction with dilutions of 1:30, but in the last days of the disease a reaction was obtained only with pure tuberculin. When a lesion was well encapsulated a dilution of 1:10 always gave a positive reaction, but when a 1:20 dilution was tried a negative reaction was the rule, especially in patients with incipient lesions. Lesions confined to the lung, and more or less advanced, gave only a faint reaction to pure tuberculin.

DWYER, Kansas City, Mo.

TREATMENT FOR CONGENITAL SYPHILIS WITH A BRAND OF ACETARSONE. J. TUSCHERER, Monatschr. f. Kinderh. **45**:63 (Sept.) 1929.

The author reports his experiences with a brand of acetarsone manufactured by the Hoechst Company. The advantage of this remedy is that it can be given by mouth. It was one of the drugs studied by Ehrlich, and it contains 27 per cent of arsenic.

A tablet contains 0.25 Gm. A course of treatment lasts forty-one days, starting in with a fourth of a tablet given once a day for three days, then twice a day for three days, then three times for three days and then four times a day. The dosage is then increased to one-half a tablet three times daily for three days and then four times daily. The following three days a whole tablet given twice daily and then three times daily for the remaining twenty days. After an interval of six weeks the course of treatment is repeated.

The results obtained by the author were fully as satisfactory as those with any other treatment.

GERSTLEY, Chicago.

IMMUNITY AGAINST TUBERCULOSIS. MAX BECK, München. med. Wchnschr. **26**: 1082 (June 28) 1929.

Beck reviews the adverse criticism of the B.C.G. vaccination by the German workers. He has obtained encouraging results in guinea-pigs by using an ointment containing attenuated human tubercle bacilli. Guinea-pigs were infected by subcutaneous injections of a virulent strain of human tubercle bacilli. A series of ten inunctions was begun in half the animals when a progressive tuberculosis had been established clinically and by microscopic examination of the enlarged lymph nodes. All the untreated control animals died of tuberculosis. None of the treated animals died of tuberculosis, and autopsies four months later failed to reveal evidence of tuberculosis in the lymph nodes or other tissues. Equally good results are reported with the prophylactic use of the ointment. The treatment of adults and children is now under way.

BRAHDY, Mount Vernon, N. Y.

Internal Diseases

BONE CAVITIES: A ROENTGENOLOGIC STUDY. E. GORDON STOLOFF, Am. J. Roentgenol. **18**:26 (July) 1927.

Bone cavities are divided into hemorrhagic conditions, i. e., expansive hemorrhagic cysts and osteitis fibrosa, and infectious conditions, which include osteomyelitis, tuberculosis, syphilis and parasitic cysts; the latter are by far the most frequent. Various conceptions of the etiology, pathogenesis and nature of bone cysts are: (1) They are degenerations of true tumors; (2) they comprise a disease entity; (3) they are associated with and are a part of the picture of what Recklinghausen called osteitis fibrosa; (4) osteitis fibrosa and osteitis deformans

(Paget) are variations of a similar pathologic process; (5) the occurrence of cysts is influenced or connected in some way with the endocrine system; (6) localized osteitis fibrosa and the generalized form are different pathologic processes; (7) there is a transition from the localized to the generalized form which is not expressed on the basis of pathologic bone, and (8) osteitis fibrosa does not comprise a disease entity, but rather a symptom complex (brown tumors, fibrous marrow and bone reconstruction) that is an expression of trauma and is localized in normal bone and generalized in pathologic bones (osteomalacia, osteoporosis and osteitis deformans). The most frequent cause of pathologic fracture in youth is bone cyst.

Pain, when present, is due to laceration or discontinuity of the periosteum. Roentgen diagnosis divides (expansive hemorrhagic) cysts into solitary, localized and multiple generalized cysts. Differential diagnosis includes giant cell sarcoma, chondroma, myxoma, metastatic carcinoma, myeloma and other types of bone cavities, such as osteomyelitis, tuberculosis and central tumors. The cortex may be expanded to a spindle or a ball and is uniformly thinned. Periosteum and joint are broken through at times, in the multiple form, in which the pathologic state (lessened resistance) of the bone is the predisposing factor. Near the cystic lesions, evidences of malacia, porosis or osteitis deformans of Paget are seen. The diaphyseal ends of the long bones in the juvenile skeleton are the sites of predilection. Case reports, a differential diagnosis and a bibliography are added.

STULIK, Chicago.

A CASE OF INFECTIOUS ILEUS OR PSEUDO-MEGALOCOLON (HIRSCHSPRUNG). BENJAMIN M. BERNSTEIN, Am. J. Roentgenol. **18**:52 (July) 1927.

A boy, aged 16, apparently well until three days before examination, developed a fever of 101 F., cough, malaise, marked constipation which resisted catharsis and enemas, and vomiting. He was asthenic; his abdomen was markedly distended; he seemed toxic and showed râles in his chest. Roentgen examination revealed a normal chest, and an enormous diffuse colon from the ileocecal valve to the rectum, with no kinking or evidence of obstruction. All symptoms, including the distention of the colon, disappeared after twenty-four hours. The author regards this as a paralytic ileus of infectious origin. Elzas reported a similar case of pseudo-ileus which he regarded as an anaphylactic reaction because of blood in the stools and subcutaneous hemorrhages. Bezy reported a case in which marked increase in size was confined to the proximal half of the colon. This type of ileus is sometimes found in typhoid, pneumonia and other severe infectious diseases, and may remain undetected.

STULIK, Chicago.

SOME EFFECTS OF ROENTGEN IRRADIATION OF THE HEART IN RHEUMATIC CARDITIS. ROBERT L. LEVY and ROSS GOLDEN, Am. J. Roentgenol. **18**: 103 (Aug.) 1927.

A review of the literature shows roentgen therapy of doubtful value for relief from cardiac pain. Postmortem observations on the heart of a patient irradiated for mediastinal Hodgkin's disease showed myocardial lesions believed to denote specific injury of the heart muscle by roentgen rays. In numerous other patients receiving irradiation for pathologic conditions of the chest and examined electrocardiographically and at necropsy, no evidence of cardiac damage was found. The authors studied twenty cases with various phases of rheumatic carditis, acute and chronic, early and late, febrile and afebrile; 139 irradiations calculated to yield 1/10 erythema dose to the heart were given. Frequent electrocardiograms were made and in fourteen cases showed changes similar to those sometimes found in the course of rheumatic fever and regarded as due to myocardial involvement. It is suggested that the alterations occurred as a result of the action of the rays on the tissues of the heart with modification of the rheumatic lesions. No changes which could be ascribed to the irradiation were found in the electrocardiograms; seventeen of the patients showed definite improvement, but the treatment is not

stressed because of the small number of cases studied and the short period of observation; eight patients had mildly unpleasant symptoms, but in no instance was there evidence of cardiac injury or an unfavorable effect on the course of the disease.

STULIK, Chicago.

ROENTGEN DIAGNOSIS AND THERAPY OF THE THYMUS IN CHILDREN. JOHN REMER and WEBSTER W. BELDEN, Am. J. Roentgenol. **18**:119 (Aug.) 1927.

The anatomy, pathology, clinical types and symptoms are described. Mors thymica, thymic asthma and status lymphaticus are mentioned. Under treatment a mortality of 33.3 per cent occurred in a series of cases in which operation was performed, while with roentgen treatment certain complications, including bronchopneumonia, appeared. In roentgen treatment, 1/10 erythema dose is advocated; the interval, preferably a week, depends on the reaction obtained. Accurate diagnosis requires flashing the tube, double intensifying screens and superspeed films. An exposure should be made while the infant is crying and another when the preinspiratory pause occurs. If there is any question of the thyroid gland receiving either direct or scattered irradiation, small doses of iodine are given three times a day for two days following each treatment.

In two cases of *Streptococcus viridans* endocarditis no change in the electrocardiograms nor any modification of the fatal progress was noted.

STULIK, Chicago.

A CASE OF CONGENITAL HYPERTROPHIC PYLORIC STENOSIS IN A MAN AGED SEVENTY-TWO. F. D. ACKMAN, Canad. M. A. J. **21**:423 (Oct. 23) 1929.

The history of the patient showed difficulty in feeding as a baby and frequent attacks of stomach trouble his entire life.

During early adult life, he had frequent attacks of colicky pain, often associated with explosive vomiting.

At 59 years there was a noticeable increase in frequency and severity of attacks until at 64 the symptoms became steadily worse. The attacks of pain usually came at night; they began with general abdominal colic, finally were localized in the epigastrium and were associated with a sensation of fulness. No medication relieved the symptoms. The patient had always been underweight.

He died of inanition. Postmortem examination revealed the typical condition of congenital hypertrophic pyloric stenosis, with atrophy of the walls of the stomach.

MOORE, Omaha.

INTRATHORACIC NEOPLASM. F. J. POYNTON, Proc. Roy. Soc. Med. **32**:1244 (July) 1929.

A boy, aged 8, was admitted to the hospital with some cyanosis and distress in breathing. A roentgenogram showed a large shadow filling the upper and anterior part of the chest. The patient improved for a time on receiving roentgen therapy. At autopsy a tumor was found, which was diagnosed lymphosarcoma.

WILLIAMSON, New Orleans.

EXOPHTHALMIC GOITRE (GRAVES' DISEASE). R. C. LIGHTWOOD, Proc. Roy. Soc. Med. **22**:1249 (July) 1929.

The author reported a case of exophthalmic goiter (Graves' disease) in a girl, aged 7½.

WILLIAMSON, New Orleans.

MACROGLOSSIA, RIGHT-SIDED: CAUSE? H. M. ODDY, Proc. Roy. Soc. Med. **22**:1250 (July) 1919.

The patient was a girl, aged 8 years, whose mother stated that the right side of the face had been swollen for years, and during the last twelve months had become more noticeable. On examination there was found a uniform enlargement

of the right side of the tongue which was quite soft. The roentgen appearance of the lower jaw was normal. Two firm knotty cords could be felt down the right side of the neck. The diagnosis lay between lymphangioma and neurofibromatosis.

WILLIAMSON, New Orleans.

SPLENIC ANEMIA. G. H. GANGE, Proc. Roy. Soc. Med. **22**:1252 (July) 1929.

A case of splenic anemia was reported in a girl, aged 6 years. On admission to the hospital, the patient looked ill; her face was puffy, and her pulse rate 140. She had marked splenomegaly with enlargement of the liver. The blood picture showed marked secondary anemia with lymphocytosis. The Wassermann reaction was negative. The direct van den Bergh test gave a delayed reaction, and the indirect a positive reaction. The temperature fluctuated between 102 and 105 F. The blood counts for the following five months are given in the report. At first the patient improved a great deal, but she did not continue to do so.

WILLIAMSON, New Orleans.

BLOOD PRESSURE IN CHILDREN. M. P. GOVIN, Bol. Soc. Cubana de pediat. **1**: 473 (Aug.) 1929.

In children, under 5 years of age, the maximum pressure was between 80 and 90 mm., and the minimum between 60 and 70 mm.; in those under 9 years, the maximum pressure was around 100 mm. The only exception was a child with nephritis whose maximum pressure was 120 mm. From 9 to 12 years, the maximum pressure was between 100 and 110 mm., with one exception. This was in a case of Fröhlich's syndrome in which the maximum pressure was 140 mm. and the minimum 90 mm.

SANFORD, Chicago.

LYMPHOSARCOMA OF THE ILEOCECAL VALVE IN A CHILD AGED FIVE. A. A. ABALLI, Bol. de Soc. cubana de pediat. **1**:497 (Sept.) 1929.

The child had no particular symptoms except an obstinate constipation. Examination showed a tumor in the lower right quadrant. The Wassermann reaction was negative, and the blood was normal. A number of roentgenograms were taken after a barium sulphate meal; these are reproduced. They showed definite obstruction and delay in emptying the bowel. Operation was performed, but the tumor was so immense that the postoperative course was fatal. Photographs of the tumor and the microscopic sections are given. These show it to be a lymphosarcoma.

SANFORD, Chicago.

FAMILIAL SPLENIC ANEMIA IN INFANCY. S'A. CARRAU and J. C. ETCHEVERRY, Arch. españ. de pediat. **13**:257 (May) 1929.

The authors report two cases of splenic anemia in twin brothers, aged 6½ months, of a family in which a third brother also had a chronic form of anemia of undetermined type.

The anemia in both cases resembled in type the pseudoleukemia of von Jaksch-Luzet.

There was a marked diminution of red cells and hemoglobin and a leukocytosis with a marked lymphocytosis.

Nucleated red cells were observed, and also some cells resembling myelocytes and megaloblasts.

There was marked splenic enlargement and hypertrophy of the liver. There were evidences of rickets, and slight fever persisted.

The authors expressed the belief that the condition was due primarily to a lesion in the hematopoietic system which developed probably during the embryonal or fetal period. The fact that it appeared in several members of a family points to a constitutional character and a definite familial tendency.

SCHLUTZ, Minneapolis.

HYDATID CYSTS OF THE LIVER AND LUNG. D. R. ROCA DE VINALS, Med. de los niños **30**:214 (July) 1929.

A boy, aged 3 years, entered the hospital with three or four tumors in the abdomen which had been diagnosed tuberculous adenitis. On palpation the abdomen resembled a sack of potatoes; small hard nodules were found and some larger ones containing fluid. The blood showed: neutrophils, 65 per cent; lymphocytes, 26 per cent, and eosinophils, 3.5 per cent. The reaction of Cassoni was strongly positive and corroborated the clinical diagnosis of hydatidosis. Four days later the eosinophils increased to 13 per cent. The child died twenty-three hours after an operation to drain the cysts in the liver. At autopsy the cysts were also found in the lung.

DWYER, Kansas City, Mo.

THE ACTION OF EUCALYPTUS OIL ON ASCARIS. E. MAHLO, Arch f. Kinderh. **87**:46 (April 19) 1929.

In studying the effect of different forms of eucalyptus oils in various dilutions, Mahlo found that most varieties caused death to *Ascaris* in a dilution of 1:250 and 1:500 in four hours. With increasing strengths, the effects diminished, until at 1:2,500 none of the eucalyptus products had any effect, while a 1:5,000 dilution of oil of chenopodium caused the death of *Ascaris* in thirty minutes.

SANFORD, Chicago.

COLITOXICOSIS OF INFANTS. B. P. B. PLANTENGA. Jahrb. f. Kinderh. **121**:156 (Sept.) 1928.

The author first reviews the clinical manifestations of the condition described at various times as cholera infantum, alimentary intoxication and, more recently, colitoxicosis. Because of its great resemblance to Asiatic cholera, search was instituted for a bacterial cause. Escherich at this time discovered *Bacillus coli* and its pathogenic properties in animals. He ascribed the etiology of cholera infantum to this organism, but died before his opinions were verified. Then the point of view changed, and Czerny's views as to constitution and nutrition gained acceptance. In 1907, Finkelstein's ideas on proper nourishment, particularly with dextrose and salts, gained acceptance.

In recent years it was demonstrated that *B. coli* invades the duodenum in this condition and the pendulum swung back to Escherich's idea. Plantenga explains the clinical condition as follows:

The colitoxin is the cause of these symptoms. However, for the growth of *B. coli* in the duodenum, the relationship between nourishment and function of the intestine is the deciding factor. When proper nutrition and digestion are impaired (by various causes, such as inanition, prematurity or parenteral ureteral infection) there is a disturbed motility and secretion in the intestinal tract and *B. coli* begins to flourish in the duodenum. Thus, *B. coli* toxin is liberated, enters the blood stream and causes the toxic manifestations.

As therapy, the immune serum (coli-paracoli serum) obtained from horses and recently prepared by Aldershoff of Utrecht is given first place. It is recommended that 20 cc. be administered subcutaneously to young infants. In addition to the serum therapy, the nourishment may be regulated (breast milk or albumin milk with 3 per cent carbohydrate). Hypodermoclysis is discarded because the poor turgor of the tissues is ascribed to infection rather than to dehydration; there is a marked improvement in turgor in the first few days following the injection of serum.

The author reports a case of alimentary intoxication of severe degree in an infant, aged 23 weeks. The therapy was 20 cc. coli-paracoli serum, with a digitalis preparation and buttermilk for nourishment. The next day showed definite clinical improvement. In three days, the cyanosis had disappeared, the pulse was much better and the tissue turgor definitely improved.

ABT, Chicago.

MUSCULAR ACTIVITY IN THE MANAGEMENT OF JUVENILE DIABETES. FRANZ HAMBURGER, München. med. Wchnschr. **26**:1329 (Aug. 9) 1929.

Hamburger calls attention to the importance of muscular activity for patients with diabetes. He found this part of the treatment mentioned only occasionally in the German literature but frequently stressed in this country. The author observed that the dextrose content of the urine was much greater at night than during the day. He also found that a patient with diabetes excreted more dextrose at rest than when he took a moderate amount of exercise. Patients in hospitals should be urged to take some suitable form of exercise as soon as they are strong enough. Hamburger's patients felt better on the days on which they were active. There is danger of hypoglycemia, however, in exercise after the administration of insulin, and it is important to inform patients of this when they are discharged from the hospital.

BRAHDY, Mount Vernon, N. Y.

DISAPPEARANCE OF A DOUBLE MITRAL LESION. A. STRÖMER, München. med. Wchnschr. **32**:1328 (Aug. 9) 1929.

Strömer reports an unusual case of recovery from a long-standing mitral insufficiency and stenosis. The patient was a woman, aged 27, in whom a diagnosis of heart disease had been made at the age of 14. During a period of three months before the author saw her, signs of decompensation were present. The patient was cyanotic, complained of dyspnea and palpitation, and had edema of the legs, hypostatic bronchitis and an enlarged liver. The apical impulse was in the sixth interspace outside the nipple line. The cardiac dulness was increased to the right and left. Loud systolic and presystolic murmurs were heard at the apex. Strophanthin given intravenously produced diuresis after one week. In three weeks the edema had disappeared; the area of cardiac dulness then decreased. Two months later the patient was well. The color was good and no abnormalities of the heart and lungs could be found. Serial orthodiagrams confirmed the decrease in the size of the heart.

BRAHDY, Mount Vernon, N. Y.

CIRRHOSIS OF THE LIVER IN CHILDHOOD AND REGENERATION OF THIS ORGAN. K. OBERHOFF, Ztschr. f. Kinderh. **47**:51 (Jan. 28) 1929.

A child, aged 4 years, in poor home conditions, developed cirrhosis of the liver, apparently without cause. The history showed no chronic infection, syphilis or tuberculosis, and disclosed measles three years before as the only acute infection. In the complete lack of other causal data, the author was tempted to consider the measles the cause of the changes in the liver, as such cases have been described. The regeneration of liver cells, he believes, takes its origin from the mesenchymal germ tissue attached to the capillary walls. An intermediate step is what are called Kupfer star cells, cells which are still morphologically vessel-wall cells, although functionally they can fulfil the duties of typical liver cells. Under physiologic conditions this reparative process is hardly detectable but it is more distinct with an increase in the load on the liver. In that condition the Kupfer cells, not yet differentiated to liver cells, take on a part of their functions and form bile. By vigorous regeneration, which sets in after marked destruction of liver tissue, and which one must assume is set up by the products of decomposition itself, one sees in the disseminated inflammatory infiltration of the supporting tissue, the transition of blood capillaries to epithelial tubules, the so-called bile duct proliferation, and further the ripening of cubicle cells to liver cells. Such regenerative proliferation tends to give to cirrhosis of the liver its peculiar character. It is especially demonstrable in cirrhosis of the liver in childhood.

EMERSON, Boston.

PAROXYSMAL TACHYCARDIA IN CHILDHOOD. FRITZ VON BERNUTH, Ztschr. f. Kinderh. **47**:94 (Jan. 28) 1929.

Three cases of paroxysmal tachycardia are described that are entirely different in their etiology and in their manner of occurrence. In the first patient the

tachycardia arose apparently from a toxic injury of the myocardium in the course of chorea. In the second case it acted like a purely nervous attack in a child with gastrocardiac complex, resulting from an operation for the immobilization of the diaphragm on the left side. This patient become better when she went to bed with a full stomach. In a third case a ventricular tachycardia was secondary to damage of the heart muscle, apparently of a degenerative nature, in a case of muscular dystrophy.

EMERSON, Boston.

Nervous Diseases

ETIOLOGY OF EPIDEMIC ENCEPHALITIS. C. LEVADITI, Arch. Neurol. & Psychiat. **22**:767 (Oct.) 1929.

Epidemic encephalitis and poliomyelitis, as well as rabies, belong to the same group of infectious diseases caused by a filtrable virus possessing an elective affinity for the nervous system. The relationship is closer, however, between the first two diseases than between either of them and rabies. They are transmitted by the same route, the nasopharynx; they are propagated by "formes frustes" and germ carriers; they are characterized by the same localization of the microbe in the central nervous system and by the same virulence of the nasopharyngeal mucous membrane. The similarity between Heine-Medin's disease and that of von Economo is so close that the experimental study of the latter was in a sense a copy of that of poliomyelitis. Nevertheless, fundamental differences between the two diseases warrant the assumption that they are due to specific viruses. These differences are clinical, anatomopathologic and experimental, and show that epidemic encephalitis and epidemic poliomyelitis are two etiologically different infectious processes, although they are caused by ultraviruses belonging to the same group of neurotropic ectodermatoses.

SANFORD, Chicago.

MENINGOCOCCUS MENINGITIS. M. JACOBI, Pediat. Bull. **1**:10 (Oct.) 1929.

Three rather unusual cases of meningitis are presented. The first was a severe meningococcus septicemia that terminated in death. There was a purulent pericarditis, pulmonary hemorrhages and cloudy swelling of the liver and kidneys. The second case showed an early fibrinous reaction in the meninges, which led to an occlusion of the foramina. The final case presented a terminal stage not usually mentioned in reference books, that of an intraventricular clot formation.

SANFORD, Chicago.

PROGRESSIVE SPINAL MUSCULAR ATROPHY OF THE WERDING-HOFFMAN TYPE. GEORGE M. LYON, South M. J. **22**:839 (Sept.) 1929.

A case of progressive spinal muscular atrophy of the Werding-Hoffman type is presented with studies of the electrical reactions of the nerves, reported for the first time. A detailed pathologic study shows the observations on the spinal cord to be distinctly different from those found in the spinal cord in poliomyelitic infections. The photograph of the patient is one of the best of this condition to be found in medical literature.

Of interest in the case are the following observations:

1. It was of a familial nature; an older brother and probably an aunt died of the same malady.

2. It occurred early in life and had an early fatal termination.

3. It was characterized by a flaccid paralysis of the muscles of the pelvic and pectoral girdles, of the back and of the accessory muscles of respiration. Proximal groups of muscles were involved first, and the paralysis advanced distally.

4. The paralysis was steadily progressive until death ensued from paralysis of the muscles of respiration.

5. The fingers and the toes were not paralyzed until relatively late in the condition.

6. The mentality was clear until the end.

7. The atrophy of the muscles was progressive, although probably hidden by subcutaneous fat at first. Toward the end, the proximal groups of muscles of the extremities and the muscles of the back were markedly atrophied.

8. The response of the nerves to stimulation over the motor points was greatly diminished early; finally, there was no response to stimulation over these points. Direct stimulation of the muscles produced a response after stimulation of the motor points gave no response.

9. The muscular atrophy was secondary to the nerve and spinal atrophy.

10. The pathologic observations showed a marked primary atrophy of the anterior horn cells of the spinal cord and of the anterior roots. The involvement of the anterior horn cells extended from the cauda equina to the medulla and was symmetrical. The degeneration of the peripheral nerves and of the anterior roots was secondary to the primary atrophy of the anterior horn cell. There was a simple atrophy of the muscles of the pelvic and pectoral girdles, of the back, of the abdomen, of the neck and of the extremities and atrophy of the accessory muscles of respiration.

AUTHOR'S SUMMARY.

TREATMENT OF CHOREA BY NIRVANOL. F. JOHN POYNTON and BERNARD SCHLESINGER, Lancet **2**:267 (Aug. 10) 1929.

Because of the numerous favorable results reported from Germany by the use of phenylethylhydantoin in the treatment of chorea, the authors were encouraged to try this drug in six cases of their own. As a result of their trial they were sufficiently impressed to bring this new form of treatment to the notice of the English medical profession in order that it might receive more general trial.

Phenylethylhydantoin was first used in 1919 by Roeder in the treatment for chorea. It has the following formula: $\begin{matrix} C_6H_5 \\ C_2H_5 \end{matrix} > C < \begin{matrix} CONH \\ | \\ NHCO \end{matrix}$ It is formed by the combination of urea and glycol, and was originally used as a hypnotic for sleeplessness and as a sedative in epilepsy and various types of psychosis. In chorea, relatively smaller doses are used, and successful results are due not to any hypnotic effect, but to a specific reaction which occurs after several days of oral administration. Some of the investigators suggest that the reaction is akin to serum disease or to a mild anaphylactic shock.

The drug is given in daily doses of 0.3 Gm. by mouth for a child aged from 9 to 14 years. In most cases, a morbilliform rash, usually accompanied by fever, appears from eight to fourteen days after treatment is begun. The drug is stopped immediately. Just before the onset of fever the choreic manifestations seem to be aggravated, but with the disappearance of the rash (usually in four or five days) they "improve with dramatic suddenness and are usually completely arrested in a week or ten days." A secondary reaction, similar to the primary one, may occur from seventeen to thirty-nine days after treatment is begun. Lesions of the heart that are present at the time are apparently not affected and "are certainly not made worse." A true eosinophilia occurs which reaches its maximum just before the appearance of the rash.

De Rudder claims that the administration of phenylethylhydantoin causes an alteration of the acid-base equilibrium of the blood; i. e., at first there is alkalosis which, at the moment of the appearance of the eruption, changes to an acidosis. Other investigators confirmed the tendency to alkalosis but were unable to demonstrate any swing to acidosis.

The authors caution against certain dangers associated with the use of the drug, among them the possibility of a deleterious effect on the bone marrow. The two patients reported to have had severe secondary reactions had received artificial sun-light therapy just after finishing a course of phenylethylhydantoin.

LANGMANN, New York.

EPIDEMIC (LETHARGIC) ENCEPHALITIS IN A VERY YOUNG INFANT. ALAN MONCRIEF, Lancet **2**:496 (Sept. 7) 1929.

The case cited is that of an infant with the history of a normal birth, and a normal physical condition up to the age of 2 weeks when irritability and progressively increasing drowsiness were noticed. The mother had been well throughout pregnancy. The infant was admitted to The Hospital for Sick Children, Great Ormond Street, at 1 month of age. On admission the child was in profound stupor. There was left facial paralysis; the pupils were contracted and fixed and the optic disks were normal. The respirations ceased on several occasions before death, but artificial respiration was effective in restoring the normal respiratory rhythm until two days after admission, when death occurred. The cerebrospinal fluid was not examined.

At postmortem examination, no gross abnormalities were found. In the optic thalamus, definite evidence of the presence of encephalitis of the "lethargica" type was found; i. e., the perivascular lymphatic spaces were full of small round cells giving the classic appearance of "cuffing."

LANGMANN, New York.

TWO EXAMPLES OF UNUSUAL DISSOCIATION OF VOLUNTARY AND EMOTIONAL MOVEMENTS IN FACIAL PARALYSIS. F. J. POYNTON, Proc. Roy. Soc. Med. **22**:1237 (July) 1929.

It is common knowledge that with an infranuclear paralysis of the facial nerve, the voluntary and the emotional movements, such as smiling, are equally diminished on the paralyzed side. The author also believes it is generally accepted that with supranuclear paralysis the emotional movements are less affected than the voluntary, but that they also in most instances are diminished on the paralyzed side. The author reported two cases which were peculiar in that the emotional movements were more obvious on the paralyzed side. One of the patients was admitted to the hospital where a diagnosis of epilepsy was made. The other was a fatal case of a rapidly growing sarcoma of the pons, involving the cerebellum.

WILLIAMSON, New Orleans.

DYSPITUITARISM WITH HYDROCEPHALUS. C. WORSTER-DROUGHT and I. M. ALLEN, Proc. Roy. Soc. Med. **22**:124 (July) 1929.

A boy, aged 9 years, was backward physically and mentally. His body and limbs were small but normally proportioned, and were well covered with adipose tissue. He weighed 35 pounds (13 Kg.) and was 36½ inches (92.7 cm.) tall. Roentgen examination showed the sagittal suture not closed, the sella turcica large and both anterior and posterior clinoid processes prominent. There was a slight shadow in the upper part of the sella turcica close to the anterior clinoid process and extending above the upper limit of the sella.

Diminished function of the anterior lobe of the pituitary is suggested by the inadequate skeletal and general growth and diminished function of the posterior lobe by the adiposity and increased sugar tolerance. The suggestion of hydrocephalus was supported by the size of the head and by the cracked pot sound on percussion.

WILLIAMSON, New Orleans.

1. MEASLES ENCEPHALITIS. 2. SYMPTOMS SUGGESTING POST-ENCEPHALITIS. D. W. WINNICOTT, Proc. Roy. Soc. Med. **22**:1247 (July) 1929.

1. The patient, aged 6, was seen on the seventh day of an attack of measles. He was taken to the hospital on Feb. 18, 1928, on account of drowsiness and abnormal behavior. Extreme lethargy persisted for twenty-two days. Toward the end of March, symptoms subsided. Early in May he was discharged, but was still weak physically and behaved abnormally. A diagnosis was made of epidemic encephalitis (lethargica).

2. The patient, aged 5, was sent to the hospital by the school medical service on account of abnormal behavior. At the age of 2 she had had an attack of measles. There was no clinical encephalitic illness, but at that time certain changes in behavior and character had developed; for example, the patient (1) talked incessantly, (2) bit and pinched, (3) would go to sleep while eating, and (4) was restless in her sleep.

WILLIAMSON, New Orleans.

PSEUDO-HYPERTROPHIC MUSCULAR DYSTROPHY IN BROTHERS. R. C. LIGHTWOOD, Proc. Roy. Soc. Med. **22**:1249 (July) 1929.

Two brothers were 10 and 3 years of age, respectively. Both were bedridden and showed generalized weakness. Both had marked pseudo-hypertrophy of the calf muscles. The diaphragm in both patients was strong. The chest showed a slight rachitic deformity in the younger patient, and a more marked deformity in the elder. In the elder brother contractures of the feet were commencing.

WILLIAMSON, New Orleans.

HYDATID CYST OF THE BRAIN IN AN INFANT. MORQUIO, Arch. de méd. d. enf. **30**:377, 1929.

In Argentina and in Uruguay, where enormous areas are dedicated to sheep raising, echinococcus disease flourishes perhaps more vigorously than in any other portion of the world. Animals dead of this disease are devoured by dogs; these in turn transmit the parasite to man, either directly or through the medium of water, vegetables or other foodstuffs. For the most part, human infestations are confined to the liver and the lungs, but improved technic, developed by continued and intensive study during recent years, has now enabled clinicians to identify the disease in many other organs. Among these, and particularly notable on account of the bizarre syndrome, is the brain. From 1902 to 1927, Morquio, at the pediatric clinic of the University of Montevideo, had the unusual opportunity of studying thirty-eight cases of hydatid cyst of the brain in infants and children. All of these patients came from country districts with easy access to both sheep and dogs; so far as known, no cases originated in the larger cities of the countries mentioned. Most of the cases of involvement of the brain were found, quite naturally, in children of the runabout age, from 5 to 11 years, and were more common in boys. In the series of thirty-eight cases, twenty-four patients were operated on, with twenty-two deaths; ten of the remaining fourteen patients died of intercurrent diseases; the result in the other children is unknown, but doubtless was fatal.

The fact that the echinococcus must traverse two capillary systems, those of the liver and the lung, before reaching the brain probably explains the relative rarity of cysts in the latter situation, but in children not only echinococcus disease by cysticercus infestation as well seems to show a predilection for the brain. In any event, clinicians in the territory involved have found that tumors of the brain affecting children are found to be cysts in at least 50 per cent of cases. Even tuberculomas are more uncommon.

Cases of the disease are described in great detail by Morquio, who offers material ranging from clinical data, with photographs and roentgenograms, to complete histories of great interest, in which the neurologic symptoms, of course, predominated.

AMESSE, Denver.

CARBOHYDRATE METABOLISM IN EPILEPTIC PATIENTS. C. J. MUNCH-PETERSON, Compt. rend. Soc. de biol. **98**:891, 1928.

In epileptic patients one sees: (1) glycosuria, with an increase of blood dextrose which does not reach the threshold necessary to cause glycosuria in normal people, and (2) with a blood sugar level of 0.18 per cent, no trace of glycosuria. These observations were made in the course of investigation of the effects of ingestion

of dextrose plus the hypodermic injection of epinephrine. In some patients, the ordinary dextrose hyperglycemia without epinephrine was as intense as with it. In fifty nonepileptic subjects, glycosuria was never observed in epinephrine hyperglycemia when this remained below the threshold value.

KUGELMASS, New York.

INFANTILE HEMIPLEGIA: TREATMENT WITH INTRAVENOUS SODIUM SALICYLATE. P. BARRY, Paris méd. **19**:158 (Aug. 17) 1929.

The author gives the illustrative case of a child, aged 6 years, who suffered from a sudden attack of coma, followed by hemiplegia. The spinal fluid was negative. Treatment was by sodium salicylate given intravenously. Twenty-three injections were made, each consisting of 10 cc. of a 10 per cent solution. Improvement began shortly after the first injection. From this and other results the author concludes that this form of treatment may be of value in allaying the infectious condition in encephalitis.

SANFORD, Chicago.

THE RELATION BETWEEN THE DEVELOPMENT OF THE NERVOUS SYSTEM AND DENTITION IN THE INFANT. G. VARIOT, Progrès méd. **93**:1197 (July 13) 1929.

Variot presents the case of a girl, aged 20 months, who has the muscle coordination of a child aged 10 months. The first teeth (median incisors) appeared at 13 months. She has nine teeth at the present time. The author believes that the retardation of the articulation and of the centers of coordination for particular movements is parallel to anomalies of embryonic modeling, such as the first tooth buds, which result in retarded dentition.

SANFORD, Chicago.

THE PSYCHOLOGY OF THE IMBECILE CHILD. J. S. GALANT, Arch. f. Kinderh. **87**: 37 (April 19) 1929.

Galant gives a report of several cases to illustrate his point that the child of subnormal intelligence is more in need of correct outside influence than is the normal child. The mind of a child of this type is much more susceptible to suggestion. A proper relationship with children's kindergartens and other environments of that sort should be sought.

SANFORD, Chicago.

GLYCOLYSIS AND THE LACTIC ACID CONTENT IN NORMAL AND PATHOLOGIC CEREBROSPINAL FLUID. H. FASOLD and H. A. SCHMIDT, Klin. Wchnschr. **8**:1532 (Aug. 13) 1929.

In 1927, Chevassut brought forward the statement that the dextrose concentration in cerebrospinal fluid decreased with increasing time. He explained this by assuming the presence of a specific glycolytic ferment in the fluid. This would be unusual, as glycolysis is associated, in general, with cellular elements.

The authors determined the dextrose and lactic acid content of cerebrospinal fluid immediately, and two, seven and fourteen days after puncture. Little change was found in normal fluid even after fourteen days. In pathologic fluid containing large numbers of cells the progressive decrease in dextrose and increase in lactic acid were marked. However, when centrifugated cell-free fluid was used, the figures for dextrose and lactic acid remained constant, showing that glycolysis in cerebrospinal fluid as well as elsewhere depends on the presence of cellular elements.

LESLIE, Evanston, Ill.

A CASE OF MIGRAINE WITH SYMPTOMS OF TETANY AND EPILEPSY. A. STROBL, Monatschr. f. Kinderh. **45**:68 (Sept.) 1929.

The author reports the case of a boy, aged 12, who had suffered from left-sided pulmonary tuberculosis and attacks of left-sided migraine since the age of 3.

Associated with the migraine were epileptic and tetany-like convulsions which were accompanied by marked secretory disturbances such as salivation and increased bronchial secretion.

The attacks were provoked by induction of pneumothorax and were helped by caffeine and a proprietary remedy.

GERSTLEY, Chicago.

THE CARDIO-INTESTINAL SYMPTOM-COMPLEX WITH PROGRESSIVE MUSCULAR DYSTROPHY: I. CLINICAL AND PATHOLOGICO-ANATOMIC OBSERVATIONS. BERBLINGER and DUKEN, Ztschr. f. Kinderh. **47**:1 (Jan. 28) 1929.

Berblinger and Duken report four cases of progressive muscular atrophy with the autopsy observations in one. All the cases are important and interesting because of the attacks involving the heart and intestines, attacks not to be found elsewhere in the literature. The first patient described would be in good condition on waking up, but later in the day would suddenly become pale and dull looking and then vomit. In another case, the course of what proved to be the last attack was so much like appendicitis that an operation was performed which revealed nothing to operate for. Intestinal symptoms were not constant, and the heart symptoms, which amounted to a tachycardia, were not complained of by the patient and so were missed. The increase in the pulse rate was insidious and often the warning of an impending attack. The authors express belief that the changes in the heart muscle are secondary and resemble only superficially those seen in the skeletal muscle in progressive muscular atrophy, and that the heart attacks may be due to disturbances of the governing centers.

EMERSON, Boston.

A CASE OF ACUTE POLIOMYOSITIS. S. VAN CREVELD, Ztschr. f. Kinderh. **47**:74 (Jan. 28) 1929.

Van Creveld reports a case of acute poliomyositis in a boy, aged 12 years, the illness beginning subacutely and secondary to a recurring catarrhal angina. One of the most important symptoms was painful swelling of the greater part of the body musculature, changing from place to place and resulting in restricted movement. The swelling was spindle shaped and at the height of the disease was characteristically hard. Other symptoms were mild fever and general weakness; other signs were edema of the skin and muscles, and in some places transient erythema, a rapid pulse rate, a distinctly palpable spleen and greatly diminished and sometimes absent reflexes, without any abnormal reflexes; there was no diminution of sensation and no reaction of degeneration. A marked eosinophilia made it difficult to rule out trichiniasis. In the course of several months the symptoms gradually disappeared, except for a mild contracture in some muscles, which receded very slowly.

EMERSON, Boston.

THE CARDIO-INTESTINAL SYMPTOM-COMPLEX WITH PROGRESSIVE MUSCULAR DYSTROPHY: II. GRAPHIC REPRESENTATION. ERWIN SCHLIEPHAKE, Ztschr. f. Kinderh. **47**:85 (Jan. 28) 1929.

In the cases of progressive muscular atrophy described by Berblinger and Duken, graphic representation of the action of the heart led Schliephake to conclusions which otherwise he could not have made. The only observations which could be made clinically were the periods of abnormal heart action in two cases in which paroxysmal tachycardia was not once suspected because of the comparatively slow rate. In a third case it was probable but not certain from the history that there had been previously an abnormal heart attack, but no conclusions could be drawn as to the kind of disturbance until an electrocardiogram had been made. This coincidence has been seldom observed, as the initial injury of the myocardium often ran along without symptoms, and attacks of cardiac distress were looked on as the result of general weakness. Schliephake expresses belief that the facts established by him and his co-worker are of basic importance in the working out of the general mechanism of muscular dystrophy.

EMERSON, Boston.

CONTRIBUTION TO POST-VACCINAL ENCEPHALITIS. R. PRIESEL, Ztschr. f. Kinderh. **47**:153 (Jan. 28) 1929.

In a case of post-vaccinal encephalitis, the appearances in the central nervous system after inoculation in a boy, aged 7 years, were looked on by Priesel as an antigen-antibody reaction. In his opinion, the typical time of onset of the encephalitis is between the ninth and the fifteenth day; the assumption of an encephalitic virus does not appear necessary.

EMERSON, Boston.

THE INTRACUTANEOUS REACTION OF MCCLURE AND ALDRICH IN CHILDREN. H. FRENKIEL and S. MANDELS, Ztschr. f. Kinderh. **47**:158 (Jan. 28) 1929.

The duration of the wheal in the McClure-Aldrich reaction was independent of the disease in different groups of children. In high grade impoverishment with water, the reaction was much hastened. On repetition the reaction showed itself as inconstant; for this reason, it is not considered a suitable clinical help.

EMERSON, Boston.

Diseases of the Ear, Nose and Throat

THE SIGNIFICANCE OF STENOSIS OF THE TRACHEA AND BRONCHI IN THE ORIGIN OF BRONCHIECTASIS. W. COURTIN, Ztschr. f. Kinderh. **47**:141 (Jan. 28) 1929.

In his studies on the pathogenesis and diagnosis of bronchiectasis, Duken has ascribed great significance to the greater kinking of the left main bronchus and its therefore narrower lumen, and he has thus explained the greater frequency of bronchiectasis in the left lung. Further, it is known that bronchiectasis arises only on the basis of chronic bronchitis, bronchiolitis or pneumonia with abscesses. Finally, Crowe was able to demonstrate in animal experimentation with artificially made strictures that dilatations came only if the bronchi became infected. All these facts are confirmed now by Courtin in the children observed by him. Therapeutically, he recommends the prevention of bronchiectasis or its extension. Children who are affected on one side only have a more favorable outlook than those who have tracheal stenosis. The attempt can be made in cases with one-sided bronchial stenosis, if the disease has not extended too far, to place the diseased side at rest.

EMERSON, Boston.

Diseases of the Skin

ROENTGEN RAY TREATMENT OF ACNE VULGARIS. JEFFREY C. MICHAEL, Arch. Dermat. & Syph. **17**:604 (May) 1928.

The author reports the cases of 191 patients with acne vulgaris who were treated by the roentgen rays and adjunct measures, and who were followed up for end-results. In no cases were permanent untoward effects from the irradiation observed; 101 patients were cured by one course of treatment; 23 were greatly improved; failure to eradicate the disease with one course of treatment occurred in 24 patients 20 of whom later reported disappearance of the disease after the treatment was discontinued; 67 had relapses, but after a second course of treatment, the final result was successful in about 85 per cent of cases. Various factors affecting the efficiency of the treatment are discussed.

SHIRLEY, Iowa City.

PARONYCHIA. H. SUTHERLAND-CAMPBELL, Arch. Dermat. & Syph. **19**:233 (Feb.) 1929.

The author attempts to prove that the etiologic factor of an epidemic of paronychia among orange workers is a "yeastlike organism," the spore form of a fungus of the family *Mucoraceae*. The skin of the orange is highly resistant

to the fungus, but the pulp is readily infected. Only those orange workers whose fingers are frequently in contact with the pulp or the juice of the orange acquire the infection.

SHIRLEY, Iowa City.

GROSS AND MICROSCOPIC CHANGES IN THE SKIN PRODUCED BY X-RAYS AND BY LIPOID SOLVENTS. LOUIS H. JORSTAD and CLINTON W. LANE, Arch. Dermat. & Syph. **19**:954 (June) 1929.

This study indicates that roentgen rays applied to the skin of the white rat in small doses cause the same type of active precancerous lesions as is produced by repeated paintings of the skin with tar preparation. Evidence is given that tar, allied substances and roentgen rays act similarly in inducing a malignant condition, in that they act as lipoid solvents.

SHIRLEY, Iowa City.

PRIMARY ACTINOMYCOSIS OF THE SKIN. FRANCESCO ROUCHESE, Arch. Dermat. & Syph. **20**:1 (July) 1929.

A case of primary actinomycosis of the skin is reported. The lesion was located on the dorsal and internal regions of the left ankle, and lasted for ten years without affecting the adjoining tissues or spreading to other parts of the body. The diagnosis was made by guinea-pig inoculation and planting on agar the material gained from the infected area of the animal. Cure was effected by total surgical removal of the affected area of skin.

SHIRLEY, Iowa City.

TREATMENT OF LEUKODERMA WITH GOLD SODIUM THIOSULPHATE. H. C. L. LINDSAY, Arch. Dermat. & Syph. **20**:22 (July) 1929.

Three cases of leukoderma are reported which were remarkably improved by the administration of gold sodium thiosulphate intravenously.

SHIRLEY, Iowa City.

THE CHLORIDE CONTENT OF THE WHOLE BLOOD IN ECZEMA. NORMAN BURGESS, Arch. Dermat. & Syph. **20**:59 (July) 1929.

The blood chlorides in twenty cases of eczema of all types including infantile eczema were found to be within normal limits. It is concluded that there is no indication for attempting to reduce the chloride of the tissues in the treatment for eczema.

SHIRLEY, Iowa City.

UNTOWARD REACTIONS FOLLOWING TOXIN TREATMENT FOR DERMATITIS VENENATA. H. J. TEMPLETON, Arch. Dermat. & Syph. **20**:83 (July) 1929.

Five cases are reported which, according to the author, demonstrate a hitherto undescribed urticarial reaction to the injection of an antigen of poison oak. The eruptions were either localized or generalized. The localized eruptions consisted primarily of urticarial wheals, the generalized eruptions of urticarial wheals and the papulovesicles of dermatitis venenata. They began within from twenty-four to seventy-two hours after injection of the extract of poison oak into patients suffering from dermatitis caused by that plant. The author believes that the desensitizing method of treatment, beginning with very small doses of the extract followed by a gradual increase, is preferable to the present orthodox method of giving large doses.

SHIRLEY, Iowa City.

TREATMENT OF ECZEMA IN INFANTS. HARRY M. ROBINSON, South. M. J. **22**: 936 (Oct.) 1929.

Milk is frequently not well tolerated by the child affected with dermatoses, notably with eczema.

Good results have been obtained in the majority of the author's cases by a milk-free replacement diet. It is desirable to hospitalize the patient, as the mothers have difficulty in enforcing the diet.

These patients always take cod liver oil well.

In one case irritation was apparently due to the milk contained in baker's bread.

SCHLUTZ, Minneapolis.

INJECTIONS OF MOTHER'S BLOOD FOR FURUNCULOSIS IN THE NURSLING. N. ALVES, Arch. de pediat., Rio de Janeiro **2**:370 (Aug.) 1929.

Furunculosis is a common infection in the nursling, and is seen more often in the infants who have their resistance undermined by digestive disturbances. It is manifested by multiple cutaneous abscesses, and is liable to grave complications. The best treatment seems to be the intramuscular injection of small quantities of maternal blood. This apparently has the power of increasing the child's resistance to the infection.

SANFORD, Chicago.

ECZEMA FROM THE STANDPOINT OF IDIOSYNCRASY. BRUNO BLOCH, Monatschr. f. Kinderh. **44**:17 (Aug.) 1929.

The author presents his views on the subject of infantile eczema. His whole theory presumes that eczema is due to an idiosyncrasy of the skin rather than to constitutional factors. The skin of an infant with eczema reacts to more irritants and to a less severe irritation than does the skin of a normal baby. The irritants are for the most part exogenous but occasionally may be endogenous in that they reach the skin by way of the blood stream.

Food has no direct influence on the eczema, but it is possible that diet may influence the skin so that the nature of the reactions may be influenced. Of course the latter might take place through all possible endogenous influences—metabolic, caloric or nervous.

There still remains a considerable group of eczemas in which there is no known etiology. Bloch believes, however, that in time even these will be found to be due to the skin's special susceptibility to some definite hitherto undiscovered irritant.

GERSTLEY, Chicago.

INFANTILE ECZEMA. E. MORO, Monatschr. f. Kinderh. **44**:45 (Aug.) 1929.

Moro divides infantile eczemas into two clinical groups. The first occurs during the first three months of life. It is seborrheic and, according to Moro, is not a true eczema. The typical infantile eczema which Moro believes is the only real eczema occurs invariably after the third month.

The author mentions one or two theories but does not lay much stress on any of them. He then advances his own idea that the disease may be due to some anomaly of mineral metabolism. The basis of this theory is in the observation that calcium occurs primarily in the cutis and potassium in the epidermis, and that light causes a distinct shifting in the relations of these two minerals. Areas of skin that are subjected to ultraviolet rays develop richness of calcium, while in the other areas calcium decreases.

GERSTLEY, Chicago.

LATE PERIODS OF EXUDATIVE DIATHESIS. G. A. ROST and P. KELLER, Monatschr. f. Kinderh. **44**:49 (Aug.) 1929.

The authors take issue, to some extent, with the theories of Jadassohn and Bloch. The latter writers lean strongly to the point of view that eczemas are primarily conditions of the skin due to external irritants. Rost and Keller mention the frequent association of eczema with asthma. Of their 150 patients with eczema 27 per cent gave a history of asthma, and 47.5 per cent either had asthma or gave a family history of that condition.

Metabolic studies are of significance. In both eczema and asthma the property of the blood to blind salicylic acid is diminished. In late eczema there is a diminution of blood dextrose which may possibly have a relation to the same process which seems to make patients with diabetes free from asthma. In both conditions there is an eosinophilia.

The authors advance these observations as arguments in favor of the hypothesis that eczema in infants is a constitutional anomaly.

GERSTLEY, Chicago.

NEVUS PIGMENTOSIS IN THE NEW-BORN. OTTO CORSDRESS, Monatschr. f. Kinderh. **45**:43 (Sept.) 1929.

The case of a new-born infant in whom almost the entire skin was covered with a pigmented nevus is given, with two illustrations. The author quotes a carefully taken family history, discusses some of the prevailing theories and shows that there is nothing in the history of the patient to corroborate any of the prevailing hypotheses as to etiology.

GERSTLEY, Chicago.

HERPES ZOSTER AFTER AN ATTACK OF CHICKENPOX. K. DIETL, Wien. klin. Wchnschr. **42**:1078 (Aug. 15) 1929.

The author cites two cases to show that herpes zoster may be an allergic reaction occurring in a person sensitized by an earlier attack of chickenpox.

In case 1, a boy, aged 13, had had chickenpox; fourteen days after being exposed to chickenpox he developed typical herpes.

In case 2, a boy who had had a mild case of chickenpox at 1 year of age, after exposure to chickenpox when 9 years of age, developed herpes zoster. It seems to the reviewer that these cases might be used as evidence against the author's thesis; i. e., that there is no connection between chickenpox and herpes.

CLAUSEN, Rochester, N. Y.

THE SENSITIVITY OF THE SKIN OF INFANTS TO IRRADIATION. KAREL SCHRUTZ, Časop. lék. česk. **65**:1158 (July 30) 1926.

The author found that the skin of an infant, aged 2 months, was 75 per cent as sensitive as the skin of an adult. It is felt that since the average dose used in children is from 50 to 60 per cent of the dose for adults, no harm results. The irradiated fields were carefully covered to prevent outside irritation, and the dose gradually increased; a slight erythema appeared after two weeks and lasted about a week. The dosage was carefully controlled with an ionometer, intensimeter and stop watch.

STULIK, Chicago.

Surgery and Orthopedics

OVARIAN TUMORS IN CHILDHOOD WITH REPORT OF FIVE CASES. THOMAS H. LANMAN, New England J. Med. **201**:555 (Sept. 19) 1929.

The author reports the five cases of ovarian tumor found in 12,260 admissions to the surgical service of the Children's Hospital, Boston, in the past ten years; he also comments thoroughly on the literature on the subject. The cases are as follows:

CASE 1.—A child, aged 11, had abdominal pain for five weeks, associated with increasing size of the abdomen. At operation, a solid tumor originating in the left ovary and broad ligament, and extending from the pelvis to the liver, was removed. The pathologic diagnosis was teratoma of the ovary. The patient died five months later with evident recurrence.

CASE 2.—Five months before examination, a child, aged 10, had persistent vomiting for six weeks; there was no marked abdominal pain, but the patient lost

weight rapidly. She was said to have passed round worms at onset. No symptoms appeared until a few days before entrance to the hospital. At operation an inoperable neoplasm was found that involved the uterus and adnexa. The pathologic report, based on removed tissue, was solid carcinoma of the ovary. The patient died one month later.

CASE 3.—A child, aged 6½, one year before examination had a severe attack of pain in the abdomen, associated with urinary incontinence; a second attack, more severe than the first, occurred three months before examination, a third, still more severe attack two weeks before examination. At operation, a cystic enlargement of the left overy was removed. The pathologic diagnosis was teratoma of the ovary. The patient was reported as perfectly well two and one-half years later.

CASE 4.—A child, aged 11, had abdominal pain of sudden onset, lasting for twenty-four hours, followed by vomiting on the morning of admission to the hospital. At operation a large right ovarian cyst was found, with pedicle twisted one and one-half times. The pathologic diagnosis was dermatocystoma (dermoid cyst) of the ovary. The patient appeared well two months later.

CASE 5.—In a girl, aged 5 months, for the past month the mother had noticed that the clothing was becoming tight; for the past week, the abdomen had been hard and tense, and on the day before entrance to the hospital there was some pain in the right lower quadrant. At operation a large mass arising from the left ovary was removed. The patient made a good operative recovery, but gradually became worse and died within two months. The pathologic diagnosis was adenocarcinoma (malignant teratoma) of the ovary.

The author stresses the necessity for early diagnosis and justifies exploration when in doubt.

GENGENBACH, Denver.

INTUSSUSCEPTION. A. SABOTTIER, Nourrisson **17**:158 (May) 1929.

Two cases are reported in infants, aged 10 and 8 months. In the first case a reduction of the invagination, which was seen early, was obtained by enemas. In the second case a laparotomy was necessary. The author emphasizes the point that medical treatment, if not immediately successful, should not be persisted in.

MCCLELLAND, Cleveland.

SURGERY AND ORTHOPEDICS IN CHILDREN DURING 1929. A. MOUCHET and C. ROEDERER, Paris méd. **29**:53 (July 20) 1929.

This is the annual review from the French literature of the progress in surgery and orthopedics for children during the past year. Some of the most important subjects are vertebral osteosynthesis, fixation of the hip and researches on tuberculosis of the extremities.

SANFORD, Chicago.

ENURESIS AND SPINA BIFIDA OCCULTA. J. JACOBOVICI, C. I. URECHIA and E. TEPOSU, Presse méd. **68**:1103 (Aug. 24) 1929.

The authors report nineteen cases of enuresis, the patients varying in age from 4 to 16. The condition was nocturnal in most instances, but two exceptions were curious. One patient was affected only when exposed to the rays of the sun for some time, and the other was troubled only when bathing. In examination of these patients, sixteen showed a small depression at the base of the spine which roentgen examination disclosed as spina bifida occulta. The remaining three cases were due to other osseous defects. The treatment is operative and consists of extradural or intradural resection. In cases that are complicated by mental retardation, the patient must be reeducated. Of fifteen patients treated by this operation, nine were cured, three were relieved, one received relief slowly, one showed no result and one died.

SANFORD, Chicago.

THE TREATMENT OF EMPYEMA (POSTPNEUMONIA) IN CHILDREN. R. DARDANI, Riv. di clin. pediat. **27**:563, 1929.

The author gives statistics regarding empyema in children treated during the last ten years in the Children's Hospital in Milan. The results are summarized in the accompanying table.

Data on Cases of Empyema at the Children's Hospital, Milan

	Cases	Deaths	Deaths, per Cent
Under 1 year	18	14	78
1 to 2 years	44	27	61
2 to 3 years	20	7	35
3 to 4 years	24	6	25
4 to 5 years	13	3	23
5 to 9 years	15	3	20
Total cases	134	60	45
Pneumococcus	88	33	37
Streptococcus	7	4	57
Left side of chest	61	25	41
Right side of chest	69	31	44
Both sides of chest	4	4	100
Tuberculous children	27	15	56
Nontuberculous children	34	13	38
Treated medically	57	30	53
Treated surgically	77	30	39
Rib resection	34	15	44
Pleurotomy	43	15	35
Vaccine therapy and operation	40	11	28
Vaccine therapy and no operation	36	13	36
No vaccine therapy; operation	37	19	51
No vaccine therapy and no operation	21	17	81

The vaccine therapy consisted of stock, mixed and autogenous vaccines, administered sometimes subcutaneously and sometimes into the pleural cavity.

Reports of several cases are given, in which sodium taurocholate was injected into the empyema cavity, by the method of Cocchi (see abstr., AM. J. DIS. CHILD. **34**:673 [Oct.] 1927), with good therapeutic results.

HIGGINS, Boston.

OPERATIVE CLOSURE OF UMBILICAL HERNIA WITH INJURY OF THE BOWEL IN A PREMATURE INFANT. J. GRUSS, Časop. lék. česk. **65**:1237 (Aug. 13) 1926.

In a premature infant weighing 2,460 Gm. and measuring 47 cm., a herniated loop of bowel was tied off in the ligature of the cord. At operation, performed within an hour, with the infant under chloroform anesthesia, the injured blood vessels were ligated and the mesentery was repaired. Resection of the injured bowel was not regarded as necessary. The navel was removed and healing was uneventful. At 1 month of age, the infant weighed 3,200 Gm. and had a clean scar which did not prolapse during crying.

STULIK, Chicago.

ACUTE GANGRENOUS APPENDICITIS WITH COMPLETE SITU INVERSUS. HNAT BELEJ, Časop. lék. česk. **65**:1340 (Sept. 3) 1926.

Classic signs of appendicitis were found on the left side in a girl, aged 10. Complete situ inversus was verified by roentgenography. On routine examination of the family, a sister, aged 12, was found to have a complete inversion of organs. In both cases no deviation from normal had been noticed by either the parents or the children.

STULIK, Chicago.

SUDDEN COMPRESSION OF THE CHEST. ARNOST GREGORA, Časop. lék. česk. **65**: 1697 (Oct. 29) 1926.

A boy, aged 15, had his chest suddenly compressed by the pressure of falling timber. He developed multiple petechial hemorrhages of the face, neck and arms

except in bands limited to the pressure of the cap, collar and arm bands. He developed a temporary exophthalmos. The mucous membranes of the mouth, pharynx and larynx were also peppered. The entire region of the petechiae was also markedly cyanotic. The only signs in the chest were several fractured ribs, with no changes in the heart or the lungs. Unconsciousness lasted for sixteen hours.

STULIK, Chicago.

Miscellaneous

ROENTGENOGRAPHY OF THE SPINE. JAMES F. BRAILSFORD, Am. J. Roentgenol. **18**:124 (Aug.) 1927.

As a general rule, more information is obtained from the lateral roentgen view than from the anteroposterior exposure, but each plane shows well marked characters in each disease. Too often the lateral picture is neglected when no gross change is shown in the anteroposterior view. Cases of spondylolisthesis, a bullet in the vertebra, and abdominal aorta aneurysm were not diagnosed because merely an anteroposterior picture was made.

STULIK, Chicago.

SUNBATHS FOR CHILDREN. LEWIS W. ELIAS, South. M. J. **22**:1003 (Nov.) 1929.

The author recommends daily sun-baths for children. Children who take them have a sense of well being.

The sun-baths tend to improve the posture of the child, on account of better muscle tone.

The children who take them are remarkably free from disease, especially head colds, and have few infections of the respiratory tract.

SCHLUTZ, Minneapolis.

CHILD BETTERMENT UNDER PROHIBITION. HAYLER, Rev. Internat. de l'enf. **8**: 522, 1929.

The author of this paper is honorary president of the World Prohibition Federation. He quotes numerous authorities in confirmation of his opinion that great improvement in the conditions surrounding child life in America has followed the adoption of the Eighteenth Amendment. Dr. Franklin H. Martin declared before the British Medical Association, in 1928, that "the foundation has now been laid for a demonstration of race betterment and extension of life that will astonish the world." In contrast to conditions prevailing in so-called wet areas, the status of the child in dry Finland and in local option districts of Scotland and New Zealand is depicted in rather rosy colors. Investigations undertaken during the past ten years in the United States are said to show a consistent rise in the social and ethical features of home life among the workers; there is an improved sense of values and a budget system which aims to support a family instead of a saloon. The bureau of vital statistics, New York City, reports a decrease of 7 per cent in neonatal deaths, 23 per cent in infants under 1 year and 40 per cent in children under 2 years for the period of 1920-1923, as compared with the years 1913-1917. "Revived ambition in the home," says Commissioner Roy Haynes of Washington, "has sent to high school and college thousands who, in our wet years, lacked the means or the encouragement to study." In 1919, the milk consumption per capita in the United States was 40 gallons; in 1923, it was 53 gallons, and in 1928, 56 gallons. Application for relief, made to the Salvation Army in slum settlements, have been reduced one-half since the prohibition law was enacted.

AMESSE, Denver.

DESTROYING A BOGEY: THE ALLEGED EXCESSIVE INFANT DEATH RATE IN FRANCE. BOURDON, Rev. Internat. de l'enf. **8**:537, 1929.

There is a firmly rooted opinion among those concerned with mortality rates that in France the figures for the period of infancy are excessively high. This has

been accounted for in some quarters on the assumption that the number of illegitimate births is unusual and that the care of these unfortunate children leaves much to be desired. As a matter of fact, illegitimacy in France reaches only moderate figures; from 1920 to 1924 there were fifteen births per thousand unmarried women between the ages of 15 and 49. This ratio is much inferior to that found in Germany and particularly to that in Hungary where there were forty-nine illegitimate births per thousand in the years 1886-1895.

With respect to the general mortality rate in infancy, statistics have been assembled by the French Committee Against Tuberculosis. These appear to show a gratifying decline during the past twenty years, and the tables quoted compare favorably with other European countries. In France there was a reduction from 159 per thousand living births in 1911 to 83 in 1927, the reports for 1928 not having been published at the time this paper was written. In contrast the rate in Spain was 127, in Hungary 185, in Scotland 89, in Germany 97, in Belgium 92, in England 68, in Sweden 52, in Australia 54 and in New Zealand 39. In the state of New York the infant death rate for 1927 was 59.

AMESSE, Denver.

THE INFLUENCE OF DAILY ROUTINE ON CHILDREN. E. SCHLESINGER, Arch. f. Kinderh. **87**:1 (April 19) 1929.

This is the second article of this series and deals with the immediate effect of gymnastic and school study. Following a standard period of exercise, measurements of strength with the dynamometer on 163 boys showed 28 per cent to be increased and 32 per cent decreased. The remainder were the same before as after. Of 113 girls, only 17 per cent showed an increase. The pulse rate was absolutely relative to the resting pulse. The blood pressure did not show much change from the systolic pressure of the rest period. There was no change in bodily temperature unless the exercise period fell in the first morning hours; then it was elevated. In the last morning hours it was decreased.

SANFORD, Chicago.

PROGRESS IN SEX EDUCATION. MAX J. EXNER, J. Social Hyg. **15**:393, 1929.

During the eighteen or twenty years of existence of the organized social hygiene movement, conspicuous progress has been made in attaining generally a higher conception of the purpose and character of sex education. A summary of the essential principles and methods serves to measure this progress.

1. Sex education places a growing emphasis on the normal and positive rather than on the pathologic and perverse manifestations of sex in human life; it aims at the individual's self-realization and a socially wholesome life.

2. Sex education, though one of the most compelling of the forces that shape personality, has come to be accepted as only a phase of character education as a whole.

3. Sex education must be (*a*) progressive from early childhood to maturity, (*b*) timely in order to be safeguarding, (*c*) graded to fit the needs of the growing child, (*d*) effective as character education by being purposeful and not merely factual and (*e*) based on example presented by the best family relationships.

4. Special courses in schools and colleges are not desirable except for the training of teachers on the subject. "The most natural and wholesome procedure is to embrace the teaching in broader subjects to which sex has a natural relation."

With progress in the sex education movement, literature dealing with the subject of sex has become increasingly scientific, and extensive research programs have been undertaken and advanced. Lectures of the type intended for students have become constructive and free from scare and sentimentality.

Among the agencies which have cooperated effectively in advancing the movement are: the student department of the International Committee of the Y. M. C. A., the Y. W. C. A., the American Social Hygiene Association, the United States Public Health Service, the Federal Council of Churches, the National Council of Parents and Teachers and the Child Study Association of America.

Details of the activities of the respective organizations over a period of years are recounted, and the growth and progress of the movement as a whole are emphasized.

The prediction is made that as a natural feature of all education for life and for citizenship, sex education has gained a momentum that will carry it well toward its goal in another decade.

GRAVES, New York.

NOTES FROM A CONSULTANT'S PRACTICE. VOGT, Deutsche med. Wchnschr. **55**:1178 (July 12) 1929.

Attention is called to the frequency with which vomiting in children may be the first, and for a time the only, symptom of the onset of meningeal disease. The author cites a case in which he was called in consultation after the patient had had repeated vomiting for about ten days and in which, by the time he saw the patient, he was able to make a diagnosis of tuberculous meningitis at once. In another case, repeated vomiting in an older child was found to be due to hydrocephalus when an ophthalmoscopic examination was made. He says that every case of vomiting in an older child in whom there are no definite signs of abdominal disturbance should arouse the suspicion of intracranial pressure. In epidemic cerebrospinal meningitis, the symptoms of onset may apparently disappear for a short time and arouse a false hope that the condition is relieved. Furthermore, Kernig's sign is not nearly so constant in children as it is in adults, nor is the rigidity of the neck so marked. The head may move freely from side to side and still be rigid forward and back. All in all, when there is any suspicion of meningitis, the examination must be complete in order to rule out this disease.

SCHERER, Duluth, Minn.

INFANT MORTALITY AND SOCIAL SERVICE IN PALESTINE. S. PELLER, Gsndhts-fürs. f. d. Kindesalt. **4**:207 (July) 1929.

The infant mortality of the Jewish population is lower than that of the Mohammedan and Christian. This is due to the superior economic and social advantages that the European Jew who has immigrated to Palestine enjoys. To date, no striking effect can be attributed to the extensive social service which is being carried on. Because of the miserable living conditions of the native population immediate relief can be secured only by a social service which has at its disposal infant homes either for day or for day and night use.

REICHLE, Cleveland.

THE FATE OF CHILDREN BORN DURING THE EXISTENCE OF A MENTAL OR NERVOUS DISEASE IN THE MOTHER. ALEXANDER PILCZ, Jahrb. f. Psychiat. u. Neurol. **46**:153, 1928.

This is the second contribution to a similar study published by Pilcz in 1924. The results are summarized as follows: Four of thirty-four children born of thirty-two mothers who were suffering from paresis were affected with congenital syphilis, whereas of six children born of tabetic mothers only one showed evidences of congenital syphilis. The mortality during the first year of life in infants born of eclamptic mothers is extraordinarily high; it would seem that after these infants have survived the first year they are, generally speaking, not in great danger of becoming affected with mental or nervous disease. The presence of a mental or a nervous disease in the mother during pregnancy is generally a serious matter for the offspring during the first year of life. Children born of mothers suffering from a mental or a nervous disorder are, up to a certain degree, in danger of being affected with a congenital psychonervous defect (feeblemindedness, ethical defect, psychopathy); nevertheless, in the author's material the number of psychonervous normal children exceeded that of defective children. The potentiality of these children to become affected psychically later in life is not any greater than is

ordinarily the case in children burdened with a psychopathic heredity. It would also appear from this investigation that epilepsy is rarely inherited directly from the mother.

KERSCHNER, New York.

ACUTE LEAD POISONING IN AN INFANT. ERNST LORENZ, Klin. Wchnschr. **8**: 1267 (July) 1929.

The author reports a case of acute lead poisoning in a child aged 5 months. One day about noon the infant was found swallowing lead bullets which had come out of a broken rattle. She seemed well the rest of the day, but was restless and cried during the night. The following day she passed numerous slimy green stools, one of which contained eight of the lead bullets. The temperature remained elevated, —38 C. (100.4 F.), the appetite poor and the stools frequent, green and filled with mucus for four days. No more bullets were passed nor could any be seen on roentgen examination. The child regained normal health within a week.

LESLIE, Evanston, Ill.

PAINFUL RELAXATION OF THE PELVIC JOINTS IN PREGNANCY. K. SKAJAA, Norsk. Mag. f. Lægevidensk., July, 1929, p. 728.

Painful relaxation of the symphysis and the sacro-iliac joints has been found in 31 of 185 private patients (16.8 per cent) at the end of pregnancy.

Concerning the etiology, the author refers to earlier investigators, such as Bar, who considered it as an osteomalacie fruste, and others, who believed it to be an abnormal decalcification going on in the last part of pregnancy. The author gives no opinion as to the real cause of such a decalcification.

He reports: (1) a number of cases in which there were slight symptoms of this lesion; (2) one case in which, after increasing pains for some time, there suddenly appeared a manifest rupture of the symphysis when the patient turned in the bed; there were also symptoms in the sacro-iliac joints; (3) three cases with symptoms of rupture, in which roentgenograms of the symphysis did not show signs of rupture — termed "pseudorupture of the symphysis," and (4) two cases showing pains and difficulty in walking, originating from one sacro-iliac joint, recurring in and increasing with each pregnancy; a lesion of the hip joint was suspected.

Roentgen examination of the symphysis was carried out in thirty-five patients without, and in nineteen patients with, painful relaxation during pregnancy. A new technic was employed, the roentgen film being placed in the vagina just behind the symphysis. The width of the symphysis in both groups was from 4 to 9 mm. In the second group, cavity formation in the cartilage was found far more frequently, while in some cases there were patches of calcic atrophy in the surrounding pubic bone and fraying on the boundary between bone and cartilage.

TOVERUD, Oslo, Norway.

Society Transactions

NORTHWESTERN PEDIATRIC SOCIETY

July 20, 1929

C. L. Moriarty, M.D., *President*

Comparison of the McClure-Aldrich Test and the Elastometer. Dr. R. E. Nutting.

The elastometer was devised by Schade for the recognition of the so-called preedematous state and to determine objectively the amount of edema present. There is a certain parallelism between the results obtained by the McClure-Aldrich intradermal saline test and the readings of the elastometer. We have found a normal elastometer reading but a decreased disappearance time of the McClure-Aldrich test. McClure has noted that the disappearance time of the McClure-Aldrich test may be normal but the elastometer shows a marked loss of elasticity. The difference between the two tests briefly stated is that the elastometer may be said to measure the degree of inhibition and fluid accumulation at any given moment while the McClure-Aldrich test rather measures the inhibition power of the tissues.

Some of our observations indicate that in cases in which there is a rapid disappearing time of the bleb, caution is to be observed with regard to the value of the Mantoux, and possibly of the Pirquet, tuberculin test.

DISCUSSION

Dr. Jeans: The McClure-Aldrich test has been used by some as evidence of vascular disorder. I should like to ask if there is any data available as to the suitability of the test for determining the circulation of any part.

Dr. Neale: What is the significance of the McClure-Aldrich test in celiac disease?

Dr. R. E. Nutting: It has been reported that when the arterial circulation is diminished, as in conditions that are likely to lead to gangrene, the McClure-Aldrich disappearing time is greatly shortened.

In celiac disease the tissues apparently have an increased avidity for water although edema may not be demonstrated.

The Relation of the Rate of Filtration to Temperature. Dr. H. M. Keith.

The experiments were performed with an apparatus especially designed for filtering small amounts of fluid. A single layer of filter paper was used as a medium. Various solutions were filtered at different temperatures. The rate of filtration through the filter paper was so irregular that no accurate quantitative comparative measurements could be made. There was a definite increase in the rate of filtration associated with the rise in temperature. This increase differed with the various solutions. (Further work is in progress and will be reported later.)

DISCUSSION

Dr. Schlutz: Would it be possible to apply this to any animal membrane in vivo? It seems to me that it would have some practical bearing on our intracutaneous therapy.

Dr. S. Amberg: These experiments were naturally undertaken with a biologic end in view. We hear much about filtration through animal membranes and take

it for granted that we are dealing with a simple, well known process. We all know that a hot solution usually filters quicker than a cool solution but the rate of acceleration has not been determined. This Dr. Keith tried to do.

We do not know enough about the filtration process itself. Dr. Keith referred to the relative independence of viscosity and the rate of filtration. It is true that if we are dealing with the same solution the rate of filtration will be related to some extent to changes in surface tension and viscosity but if we take other solutions it is a different story. Undiluted blood serum filters at about the same rate as caseinogen or gelatin solutions in concentrations of 1:10,000 whereas mucin filters more slowly and the surface tension of 1:1,000,000 is about that of water and so is its viscosity while the rate of filtration is considerably slower. We have done some experiments on the mesentery of the frog which also showed a definite slowing with cool solutions and acceleration when warm solutions were filtered.

ANOMALIES OF THE URINARY TRACT IN INFANTS. DR. A. S. HURT.

This article was published in the December issue, **38**:1202, 1929.

DISCUSSION

DR. H. F. HELMHOLZ: The question of whether or not a urinary anomaly predisposes to infection is of the utmost importance in a study of this kind and its relationship to urinary infection in the infant. In fact, we are working at the present time to determine the incidence of pyuria during the first year of life and whether or not these urinary anomalies predispose to infection. We have to distinguish sharply between a predisposition to infection and inability to cure infection after it has taken place. We know that once an infection has become established in the urinary tract it is practically impossible to clear it up when there is an anomaly.

DR. SCHLUTZ: I wish to call attention to a remark made by Dr. Hurt that these conditions can be overlooked, and are probably easily overlooked by the practitioner. I recall one case that occurred at the University Hospital within the last four months and I am sure it is not included in this series since Dr. Hurt's service preceded this period. This infant, of about 2½ months of age, was brought in because of hematuria and complete anuria which had lasted for almost two weeks. I am under the impression that there was no pyelitis. There was bilateral hydronephrosis. The child died, and the case came to autopsy. It seemed remarkable to me that the condition had not been recognized earlier.

DR. ANDREWS: I saw an interesting case about four days ago although it does not apply here entirely. The child was about 4 months of age and we were unable to determine its sex. The parts have developed sufficiently so that we have decided that it is a male child. The urethral opening is about 1 inch (2.5 cm.) below where it should be normally.

DR. C. L. MORIARTY: I should like to ask Dr. Helmholz what proportion of persistent pyelitis in the new-born infant is thought to be due to abnormalities.

DR. H. F. HELMHOLZ: I do not know of any figures bearing on that question. I think that we have seen three or four here in the last year or two. One had a definite abnormality—a cord bladder. Most of the cases clear up readily.

DR. A. S. HURT: I might say that I did not include those cases which were accompanied by multiple anomalies—monstrosities, and so forth—which were incompatible with life. In the last case only there was a second anomaly, a defect in the interventricular septum of which the child apparently died.

THE AMOUNT OF AMMONIA GIVEN OFF BY PROTEIN SOLUTIONS. DR. S. AMBERG.

When protein is exposed to the action of rather strong alkali at room temperature, ammonia is given off. Different proteins give off varying amounts of

ammonia under about equal conditions. (This work is in progress and will be reported in detail later.)

ARTERIOVENOUS COMMUNICATION: REPORT OF A CASE. DR. K. B. GEDDIE.

A girl, aged 8 years, came to the clinic because of swelling of the right leg and knee. The right leg had been larger than the left since birth. Two years before she had fallen and injured the right knee slightly. An infection had developed which was diagnosed as "blood poisoning." Five days later, the knee, leg and thigh to the hip had become swollen, red and painful. At this time, scarlet fever had been diagnosed because of a rash on the abdomen even though there was no vomiting or pharyngitis, and the rash was limited to the abdomen. About three weeks after the injury the swollen region about the knee had opened spontaneously and had drained a large amount of pus for about one month, after which the leg had returned to almost its normal size. Recently, there had been progressive increase in the size of the leg, the swelling being more marked in the evening.

Physical examination was essentially negative except for the right lower limb which was grossly larger than the left. The circumference in the upper third of the thigh was 1 cm. greater, in the lower third 3.5 cm. greater and in the calf 2.5 cm. greater on the right than on the left. There was no alteration in length, limitation of movement, pitting edema, varicosities or tenderness. The skin was thickened, somewhat indurated and hard and was of the pig skin type. There was no thrill or bruit. The superficial temperature was 2 degrees higher on the right than on a corresponding point on the left leg. The systolic blood pressure was 90; the diastolic, 62. The venous blood from the vein of the right ankle was distinctly brighter than that taken from the vein of the arm.

The diagnosis, therefore, was arteriovenous communication.

CONGENITAL CYST OF THE LUNG: REPORT OF A CASE. DR. S. W. MORGAN.

A boy, aged 3½ months, was brought to the hospital. The birth had been spontaneous. The birth weight was 3,270 Gm. Examination at birth revealed no abnormalities. Ten days later he had developed bilateral otitis media. The ears had discharged for two weeks after myringotomy. From then until admission to the hospital he had had two more attacks of otitis media. The mother had noticed that since birth there were times when the infant would give an expiratory grunt.

The infant was brought to the hospital because of restlessness, loss of appetite, rapid breathing and fever which had begun about a week before and had grown progressively worse. Examination showed him to be pale and undernourished, weighing 4,220 Gm. Respirations were rapid. Occasional râles were heard posteriorly over the upper lobe of the right lung, and there was dulness over the lower lobe of the same lung. The rectal temperature was 103 F. Urinalysis gave negative results. The blood showed: hemoglobin, 45 per cent; erythrocytes, 3,490,000, and leukocytes, 24,600, with 77 per cent neutrophils, 19 per cent lymphocytes and 4 per cent transitionals. The first roentgenogram of the chest revealed numerous small cavities in the right lung. Later pictures showed that these had merged into one cavity. Congenital cyst of the lung with infection was diagnosed.

During the patient's stay in the hospital, the temperature ranged from normal to 104 F. He developed another attack of otitis media. He was discharged after thirty-eight days, the temperature being normal. Subsequent communication indicated that the infant was apparently normal, except for an occasional slight cough.

Congenital cyst of the lung is a rather rare congenital anomaly. The total number of cases reported in the literature amounts to 114. Most of the cases are reported in the German literature. In reviewing the age of death in 104 cases reported by various authors, 29 patients died before the age of 1 year, 17 died

between the ages of 1 and 15 years and 49 reached adult life. One patient lived to be 84 and died of apoplexy. Of these 104 patients, 42 had clinical signs referable to the lungs.

DISCUSSION

DR. NEALE: I should like to ask Dr. Morgan if there is any particular reason why the condition is noted in the right lung. I have seen one patient in London and two cases in Boston. They were interesting as at operation the cysts each contained what appeared to be gastric juice enzyme and free hydrochloric acid. They apparently developed from the stomach and were isolated in the posterior mediastinum and pushed the heart over. One patient died and one is completely cured. The wall of the cyst was curetted out and the wound healed of its own volition.

DR. S. AMBERG: We had an interesting case which possibly falls into this group; a child, aged 7 years, came in with a pneumothorax. At operation Dr. Hedblom found what was regarded as congenital absence of the right lung, but in looking up the literature at that time we found that in congenital absence of the lung there is no pneumothorax. There were no such cases in those which Dr. Hedblom had collected up to that time. This might have been a cyst which in the course of events gave rise to a pneumothorax.

DR. SCHLUTZ: We had a case at the University Hospital about two years ago in which there was connection with the esophagus, and the most pronounced symptom in the case was immediate cyanosis on feeding. The case came to autopsy and was reported in the ARCHIVES in 1928. These cysts, I think, are probably bronchogenic and in most instances have connection with the esophagus.

DR. S. W. MORGAN: The 114 cases reported in the literature were fairly evenly divided as to the side of the lung, and the males and females were about equal. The small cysts showed a columnar epithelium in layers. The larger cysts were of a cuboidal epithelium. Although most of the cysts contained fluid, no mention was made of the type except in cases in which the connection was with the esophagus. In these there were gastric enzymes.

RENAL CHANGES FOLLOWING INTRAVENOUS ADMINISTRATION OF SUCROSE. DR. H. F. HELMHOLZ.

Intravenous injection of hypotonic sucrose solution produces marked diuresis in the rabbit. A single injection produces slight swelling of the kidney and marked histologic changes in all the cells of the convoluted tubules. The changes are characterized by swelling of the cells and the appearance of large vacuoles in the protoplasm. Repeated injections cause marked swelling of the kidney which is brownish red, soft and edematous. Histologically, the convoluted tubules are almost obliterated by the cells which are greatly swollen with almost clear protoplasm and pyknotic nuclei. The renal tissue resembles that of a hypernephroma. The Malpighian corpuscles show practically no change. After repeated injections there is a definite lowering of the power of the kidney to excrete water. (Preliminary report of work to be published in detail later.)

DISCUSSION

DR. SCHLUTZ: Would a solution weaker than 20 per cent cause such a reaction? In what strength can it be given?

DR. ANDREWS: How often did you repeat these injections?

DR. H. F. HELMHOLZ: We are working at present on the problem regarding the strength of the solution, that is, giving 10 per cent or weaker solution and increasing the amount of fluid so that there is the same amount of sugar in a weaker solution. We tried to accomplish the same thing by putting physiologic solution of sodium chloride into the peritoneal cavity. We found that if we used 0.4 rather than 0.8 per cent it was more readily available for excretion.

These injections were started out every forty-eight hours but we lost so many rabbits that we had to increase the interval, and the injections were usually given at intervals of from three to four days. We found that sufficient time for a recovery of the ear vein. It is sometimes necessary to inject into two veins when larger amounts are used. Twenty per cent solution is rather syrupy and runs in slowly.

DR. HUENEKENS: Are these permanent changes from one injection? When you get these changes are there clinical changes?

DR. H. F. HEMHOLZ: Apparently there are no clinical changes. We have made a number of phthalein tests after one, two and three injections and there are no changes in the excretion. All of the determinations of the water metabolism are rather difficult, and we are working now on some definite technic by which to determine an adequate water test for a rabbit. It is difficult to give him a large amount of fluid per os. We do not know what the normal animal will excrete when physiologic solution of sodium chloride is given in large amounts by vein or peritoneum.

REPORT OF TWO CASES OF VON RECKLINGHAUSEN'S DISEASE. DR. C. C. STEWART.

CASE 1.—A boy, aged 11 years, came to the clinic because of a recurrent growth on the right arm. His family and past medical history was irrelevant. The parents had noticed a red mark on the inner surface of the right arm when he was 9 months old. This had grown to the size of a lemon and had been excised when he was 7. It had recurred soon and had grown especially fast in the last year. The arm ached after exercise, and there were occasional sharp pains in the tumor.

He was only 53 inches (134.6 cm.) tall and was 7 per cent underweight. He was normal mentally. A soft mass, tender to pressure in certain places, occupied the inner aspect of the lower two thirds of the right arm, which was 5 cm. larger than the left. There were irregular, twisted cords of firm tissue palpable in the soft mass. The overlying skin was pinkish brown, of coarse texture and adherent to the tumor. Four soft, elevated areas the size of nickels were found on the back and left hip. Numerous irregular cafe au lait patches were seen on the trunk. Dr. Learmonth removed a neurofibroma weighing 180 Gm.; it arose from the median nerve, but also connected with two branches of the internal cutaneous nerve. The musculospiral nerve also was affected by fibromatosis.

CASE 2.—A boy, aged 8 years, came to the clinic because of deformity of the chest and a soft mass on the back. Six brothers and two sisters were living and well. He had been slow in learning to sit and walk. A soft, painless lump had appeared over the posterior right thorax four years before. This had grown slowly at first but more rapidly later, he had begun to walk bent over several months before. His general health had always been good.

Examination in the orthopedic section revealed lower dorsal right scoliosis with a soft tumor mass over the already prominent right posterior side of the chest. Twisted, wormlike cords of firm tissue were palpable in the soft mass. The overlying skin was pigmented, and there was a large cafe au lait patch on the left side of the abdomen. Osteochondritis with scoliosis and von Recklinghausen's disease were diagnosed. He was given a Taylor back brace.

Both patients had marked excessive pigmentation of the skin and cutaneous neurofibromas. Of the other four forms in Thomson's classification, the first case had multiple neuromas of at least the musculospiral nerve. The main tumor was not typical of any of these groups, arising as it did from a nerve trunk but feeling and appearing more like a plexiform neurofibroma. A secondary sarcoma was feared but was not present. The large tumor in the second case was a plexiform neurofibroma or possibly it may have been of the elephantiasis neuromatosa type. It is questionable whether the scoliosis had any connection in this case with the von Recklinghausen's disease.

DISCUSSION

DR. HUENEKENS: I should like to ask whether the tumor was removed entirely or if there is likely to be a recurrence.

DR. C. C. STEWART: The fact that the disease is one which may involve many nerves makes a statement in regard to recurrence problematic.

REPORT OF A CASE OF ACUTE LYMPHATIC LEUKEMIA AND A CASE OF MECKEL'S DIVERTICULUM (DEMONSTRATION OF PATHOLOGIC SPECIMENS). DR. R. L. J. KENNEDY.

CASE 1.—A child, whose past history revealed nothing of importance, was visiting with relatives in Illinois when she became ill with headache and fever. On the third day, it was noted that she had some enlargement of the cervical lymph nodes although it was not particularly striking. On the fourth day, the father decided to return to Rochester and drove there, arriving about 3 o'clock in the morning of the fifth day. The patient's condition did not change during the trip. A local physician saw her and took cultures of the throat. Later the father noticed that she was having difficulty with the right leg. Shortly before noon of the fifth day she developed generalized convulsions and stiffness and became cyanotic. She grew rapidly worse and was brought to the hospital the latter part of the afternoon in a dying condition. She gasped a few times after entrance and then died. There was rather deep cyanosis. We were at a loss to know what the condition might have been, although it was felt in a general way that she was suffering from an infection which had suddenly become overwhelming and was probably accompanied by cerebral involvement.

At necropsy numerous petechiae and hemorrhages were found in the omentum, mesentery, parietal and visceral peritoneum, visceral pleura and lung substance. Numerous hemorrhages were seen in the mucous membrane of the stomach. A few petechiae were present in the tissue of the kidneys, pelves and ureters. There were three small hemorrhages in the mucous membrane of the bladder. The lymph nodes, especially in the cervical and occipital regions, in the hilum of both lungs, in the mesentery and about the greater curvature of the stomach, were enlarged. The brain showed increased pressure with considerable bloody fluid in the ventricles. Although no hemorrhage was visible on the surface both cerebral hemispheres on cutting showed innumerable areas of hemorrhage. Microscopic examination of one of the numerous punctate hemorrhages scattered throughout the tissue revealed extensive leukoblastic infiltration, mostly perivascular. Blood taken after death showed observations typical of acute lymphatic leukemia.

CASE 2.—An infant, aged 21 months, whose history was irrelevant until seventeen days before admission, had suffered from an attack of influenza. She seemed to make a good recovery. Seven days later she developed an eruption which was said to have been typical of measles. She had had fever from 100 to 103 F., although it was occasionally not very high. On the fifteenth day, she had apparently recovered from the measles, but purpuric spots had begun to appear and she had passed some blood by rectum both with and without fecal material. This had persisted for two days. She had become quite weak when admitted to the hospital.

There were purpuric spots over the entire body and oral mucous membrane. The hemoglobin was 28 per cent; the erythrocytes numbered 1,800,000. The white count was 4,800, with 128,000 platelets. The bleeding time of seven and ten minutes was apparently normal. The platelet count was rather low. She was given a transfusion of 120 cc. intravenously and was given coagulin and thromboplastin. The second day the blood in the stools seemed to be decreased and the child seemed to be improved but she went rapidly downhill and died the following day. The condition was thought to be acute infectious purpura.

At necropsy a few petechiae were found in the pericardium, endocardium, pleura of both lungs and bladder. The mucosa of the stomach was completely

covered with hemorrhagic areas from 0.2 to 1 cm. in diameter. There was a Meckel's diverticulum 52 cm. from the ileocecal junction measuring 1.2 by 2 cm. There were numerous scattered hemorrhagic areas on the serosal and mucosal surfaces of the colon and rectum. The only histologic data of importance were in the Meckel's diverticulum which showed extensive submucosal hemorrhages, one of which extended throughout the wall from mucosa to serosa.

FULTON COUNTY MEDICAL SOCIETY, ATLANTA, GEORGIA

Oct. 10, 1929

LEE BIVINGS, M.D., *Chairman*

PERNICIOUS ANEMIA. DR. W. WILLIS ANDERSON.

L. H., aged 8 years, a congenital deaf mute, was admitted to Wesley Hospital on Nov. 22, 1928, with a note from the deaf and dumb school she was attending, that she had hookworm and malaria. Her mother had died several years before and her father had deserted her, so that a family history could not be obtained.

She had been under observation in the deaf and dumb school for a period of one year. During that time, she had been very pale, had had intermittent fever at intervals and had spent considerable time in the school infirmary.

On admission to the Wesley Hospital, she had anemia and her color was lemon yellow. The right epitrochlear gland was just palpable, but there was no other general glandular enlargement. There was a faint systolic heart murmur over the body of the heart, but no cardiac enlargement. The spleen was three fingerbreadths below the costal margin in the left mammary line, and the liver was two fingerbreadths below the costal margin in the right mammary line. The stools were examined frequently for intestinal parasites, and numerous smears were made from the blood for malarial parasites. The Wassermann reaction of the blood was negative, and roentgen examination of the chest revealed nothing of note. Examination of the blood on admission to the hospital showed: red blood cells, 3,760,000; white blood cells, 6,650; hemoglobin, 60 per cent; polymorphonuclears, 40 per cent; small lymphocytes, 36 per cent; large lymphocytes, 16 per cent; eosinophils, 4 per cent, and transitionals, 4 per cent. On December 5, the blood picture showed: red blood cells, 2,780,000; white blood cells, 5,450; hemoglobin, 64 per cent; polymorphonuclears, 60 per cent; small lymphocytes, 28 per cent, and large lymphocytes, 12 per cent.

She spent two weeks in the hospital during her first visit. She had a slight fever at intervals of from 99 to 100 F., which on two occasions rose to 102 F. She was given general tonic measures, including a balanced ration, sunshine and reduced iron. In spite of the negative results of the examination of the stool, she was given two treatments for intestinal parasites without avail.

She returned to school two weeks after admission with instructions to continue the foregoing general tonic measures. Again, she made no marked progress at school and reentered the Wesley Hospital on Feb. 28, 1929. On March 1, the blood picture showed: red blood cells, 1,940,000; white blood cells, 13,700; hemoglobin, 50 per cent; polymorphonuclears, 72 per cent; small lymphocytes, 20 per cent, and large lymphocytes, 8 per cent. A stained smear examined by Dr. Kracke showed changes typical of a severe anemia, many nucleated red blood cells, much polychromatophilia, anisocytosis and poikilocytosis, with increased percentage of immature polymorphonucleated cells, all indicating a severe anemia with degeneration of the bone marrow. The blood at this time was typical of pernicious anemia. The rest of the laboratory examinations, including the Wassermann test and numerous examinations of the stool and blood, revealed nothing else of note.

The child was then treated for pernicious anemia, receiving 200 Gm. of cooked liver a day, with 120 Gm. of muscle meat a day, together with fruits, milk and a generally balanced ration. The anemia began to improve almost at once. On March 12, the blood picture showed: red blood cells, 3,480,000; white blood cells, 9,300; hemoglobin, 60 per cent; polymorphonuclears, 34 per cent; small lymphocytes, 53 per cent; large lymphocytes, 9 per cent, and eosinophils, 4 per cent. On March 19, red blood cells, 4,440,000; white blood cells, 7,950; hemoglobin, 80 per cent; polymorphonuclears, 41 per cent; small lymphocytes, 54 per cent and large lymphocytes, 5 per cent. On March 28: red blood cells, 4,400,000; white blood cells, 9,250; hemoglobin, 80 per cent; polymorphonuclears, 36 per cent; small lymphocytes, 57 per cent; large lymphocytes, 4 per cent, and transitionals, 3 per cent.

During this time other medication was discontinued. The child's weight increased very rapidly. On March 7, she weighed 42 pounds (19.1 Kg.) and on April 13, 56 pounds (25.4 Kg.). Although she has not been examined since that time, written reports from her school state that she is in good condition.

Book Reviews

PHYSICAL EDUCATION IN INFANCY AND ADOLESCENCE. By M. BOIGEY. Price, 20 francs. Pp. 252. Paris: L'Expansion Scientifique Francaise, 1929.

This book is one of the group on infantile pathology and deals with the methods and advantages of physical education in childhood. The author believes that physical exercise improves the physiologic as well as the mental functions. The first chapters are devoted to a discussion of this fact. For infants he advocates exercises such as bending and stretching of the limbs to begin at 3 months. The preschool child is able to take regulated gymnastics, and for the adolescent the more strenuous games such as push ball, football and hockey are advocated. The final chapter on biometry contains some interesting statistics on groups of children before and after standardized groups of exercise. A good bibliography of the French literature on this subject has been added. The book is well bound in paper as are all this series. This should be of interest to the clinician, because it shows how well directed and supervised are the general physical exercises abroad, compared to the rather haphazard direction in this country.

THE DEVELOPMENT AND GROWTH OF THE EXTERNAL DIMENSIONS OF THE HUMAN BODY IN THE FETAL PERIOD. By R. E. SCAMMON and L. A. CALKINS. Price, $10. Pp. 365, with 73 figures and 70 field graphs. Minneapolis: The University of Minnesota Press, 1929.

This book is a report on a systematic, quantitative study of the growth and structure of the body during the fetal period. The material is based on 35,000 determinations of 71 external dimensions of the body on a series of 400 selected human fetuses. Special studies were made to show also the effects of molding at birth and the artefacts produced by preservation in formaldehyde. One of the most important results of this work is the establishment of a new principle, that in general the linear growth of the various parts of the body is in uniform ratio during the fetal period. The wealth of original data and the critical discussion make this an indispensable work of reference to all who are concerned with the problems of growth. The book is well bound and well printed, and the paper is of excellent quality.

RICKETS. By G. BARRAUD. Price, 18 francs. Pp. 180, with 11 figures and plates. Paris: L'Expansion Scientifique Francaise, 1929.

This book is one of the series on infantile pathology. It is not intended as an extensive textbook on rickets, but as a résumé of the latest developments in its study. The first part is devoted to the symptoms and various forms of rickets. Rickets associated with syphilis, tuberculosis and scurvy are described with more detail then is usual in American textbooks, probably due to their greater frequency. The same is true of the rickets of preschool age "rachitsme tardif." The second part deals with the history and cause of rickets, and the final part with treatment. This is discussed rather fully, particularly the therapeusis. A broad point of view is taken on treatment with irradiated foods; the author believes that the accepted methods of treatment should not be abandoned for these newer methods. This book is well bound in paper, and the photographic plates are well produced. It should be of interest to the clinician for its comparison to American ideas, and to the student for its compactness.

ALIMENTARY DISTURBANCES OF INFANCY. By G. MOURIQUAND. Price, 18 francs. Pp. 180. Paris: L'Expansion Scientifique Francaise, 1929.

This book is one of the series on infantile pathology and deals with alimentary disturbances. The first chapter deals with the nutrition of the normal infant. The second and third discuss the common digestive disorders and the fourth and fifth vitamin deficiency. The last two chapters are interesting and are devoted to anemias caused by nutrition, and nutrition in arthritis. It is refreshing to see such importance put on a proper diet as a prophylaxis against these more unusual conditions. The book is bound in paper, but the printing is good. It should be of interest to the clinician for its broad point of view, and to the student for its conciseness.

Directory of Pediatric Societies

INTERNATIONAL

International Pediatric Congress

Prof. I. Jundell, Artillerigatan 23, Stockholm, Sweden.
Place: Stockholm. Time: Aug. 17-20, 1930.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman: Dr. William Weston, 1231 Bull. St., Columbia, S. C.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Place: Detroit. Time: June 23-27, 1930.

American Pediatric Society

President: Dr. Joseph Brennemann, 30 N. Michigan Blvd., Chicago.
Secretary-Treasurer: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Place: Windsor Hotel, Montreal. Time: June 2-4, 1930.

The Association of American Teachers of the Diseases of Children

President: Dr. Lawrence T. Royster, State Board of Health, University, Va.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.

American Child Health Association

President: Hon. Herbert Hoover, 370 7th Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 7th Ave., New York.

Canadian Society for the Study of Diseases of Children

President: Dr. Thomas Crossan Clark, 51 Herkimer St., Hamilton, Ont.
Secretary-Treasurer: Dr. Frank H. Boone, 164 James St. S., Hamilton, Ont.

SECTIONAL

Central States Pediatric Society

President: Dr. Edward Clay Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Blvd., Chicago.
Place: Memphis, Tenn. Time: Fall, 1930.

Section on Pediatrics of Southern Medical Association

Chairman: Dr. H. Leslie Moore, 1717 Pacific Ave., Dallas, Texas.
Secretary: Dr. Ludo von Meysenbug, 3501 Prytania St., New Orleans, La.
Place: Louisville, Ky.: November, 1930.

LOCAL

Alabama Pediatric Society

President: Dr. J. MacBell, Mobile.
Secretary-Treasurer: Dr. Hughes Kennedy, Jr., Highland Plaza Apts., Birmingham.

Northern California Pediatric Society

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

Southwestern Pediatric Society

President: Dr. Ezra S. Fish, Pacific Mutual Bldg., Los Angeles.
Secretary: Dr. Fred L. Glascock, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

The Rocky Mountain Pediatric Society

President: Dr. Elsie Seelye Pratt, Republic Bldg., Denver.
Secretary-Treasurer: Dr. Wilford W. Barber, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

Georgia Pediatric Society

President: Dr. W. N. Adkins, Medical Arts Bldg., Atlanta.
Secretary-Treasurer: Dr. E. N. Gleaton, 212 E. Gaston St., Savannah.

Pediatric Section of Fulton County Medical Society, Atlanta, Ga.

Chairman: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Secretary: Dr. William Kiser, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

New England Pediatric Society

President: Dr. Edwin T. Wyman, 483 Beacon St., Boston.
Secretary-Treasurer: Dr. Randolph K. Byers, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

Chicago Pediatric Society

President: Dr. Arthur H. Parmelee, 310 S. Michigan Blvd., Chicago.
Secretary: Dr. Bert I. Beverly, 130 S. Oak Park Ave., Oak Park, Ill.
Place: City Club. Time: Third Tuesday of each month.

Louisiana State Pediatric Society

President: Dr. J. A. Crawford, Lake Charles.
Secretary-Treasurer: Dr. C. T. Williams, 7401 Burthe St., New Orleans.

Detroit Pediatric Society

President: Dr. Wyman C. C. Cole, 2970 W. Grand Blvd., Detroit.
Secretary: Dr. Charles A. Wilson, 71 E. Perry St., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. W. D. Lyon, 101 S. Balch St., Akron, Ohio.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor, Mich. Time: About July 15, 1930.

Northwestern Pediatric Society

President: Dr. C. R. Moriarity, La Salle Bldg., Minneapolis.
Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Place: University Campus and Rochester, Minn. Time: Winter, Spring, Summer, Fall.

St. Louis Pediatric Society

President: Dr. Park J. White, Beaumont Bldg., St. Louis.
Secretary-Treasurer: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

Nebraska-Iowa Pediatric Society

President: Dr. H. B. Hamilton, 434 Aquila Court Bldg., Omaha.
Secretary: Dr. George L. Clark, 1817 Vinton St., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive, 6 p. m.

Brooklyn Pediatric Society

President: Dr. Louis M. Ruderman, 961 Eastern Pkwy., Brooklyn.
Secretary: Dr. Joseph F. Paulonis, 1357 Buschwick Ave., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Bronx Pediatric Society

President: Dr. L. H. Barenberg, 1749 Grand Concourse, New York.
Secretary: Dr. Joseph Golomb, 496 E. 175th St., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. F. Elmer Johnson, 300 West End Ave., New York.
Secretary: Dr. Hugh Chaplin, 39 E. 75th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Rochester Pediatric Society

President: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Howard F. Rowley, 278 Alexander St., Rochester, N. Y.
Place: Arranged by program committee. Time: First Friday of each month from October to May.

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. John Toomey, Cleveland City Hospital, Cleveland.
Secretary: Dr. A. B. Grossman, 7016 Euclid Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Oklahoma State Pediatric Society

President: Dr. William M. Taylor, Osler Bldg., Oklahoma City.
Secretary: Dr. Carol Pounders, 110 W. 10th St., Oklahoma City.
Place: Shawnee. Time: May, 1930.

Philadelphia Pediatric Society

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. Zaccheus R. Scott, Westinghouse Bldg., Pittsburgh.
Secretary: Dr. Theodore C. Elterich, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months.

The South Carolina Pediatric Society

President: Dr. E. A. Hines, Seneca.
Secretary-Treasurer: Dr. R. M. Pollitzer, 105 E. North St., Greenville.

Memphis Pediatric Society

President: Dr. G. J. Levy, 899 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. R. Graves, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Texas Pediatric Society

President: Dr. H. P. Ledford, 1310 9th St., Wichita.
Secretary-Treasurer: Dr. John G. Young, 3930 McKinney Ave., Dallas.

Richmond Pediatric Society

President: Dr. J. B. Stone, 2042 Park Ave., Medical Arts Bldg., Richmond, Va.
Secretary-Treasurer: Dr. Samuel A. Anderson, Jr., 2326 W. Grace St., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St. Time: First Thursday of each month (other than during the summer).

Virginia Pediatric Society

President: Dr. Franklin D. Wilson, 136 York St., Norfolk.
Secretary: Dr. J. B. Stone, 2042 Park Ave., Richmond.

North Pacific Pediatric Society

President: Dr. W. F. Patrick, Medical Arts Bldg., Portland, Ore.
Secretary: Dr. L. Howard Smith, Medical Arts Bldg., Portland, Ore.

Seattle Pediatric Society

President: Dr. Vernon W. Spickard, Cobb Bldg., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Milwaukee Pediatric Society

President: Dr. M. G. Peterman, 167 17th St., Milwaukee.
Secretary: Dr. F. R. Janney, 418 E. North Ave., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. G. A. Davis, 12 Belsize Drive, Toronto.
Secretary: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Time: November 17, December 15, February 16 and March 15.

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